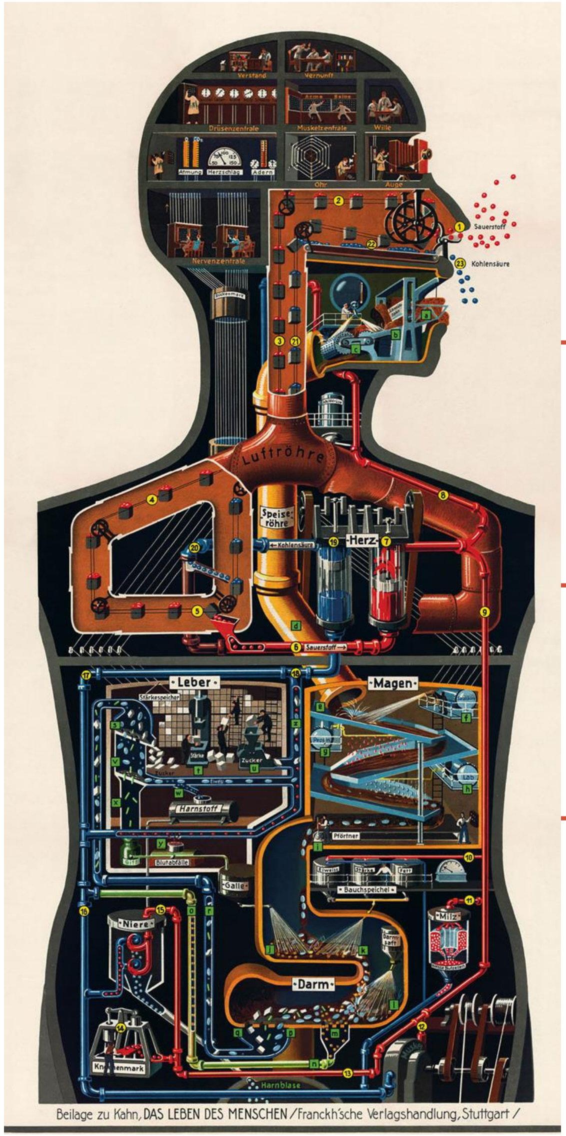


Fritz Kahn (1888 – 1968)

BIOMECHANICS

2: Physiology of Cardiovascular, Respiratory and Renal system

7ο εξάμηνο

Σχολή Μηχανολόγων Μηχανικών ΕΜΠ

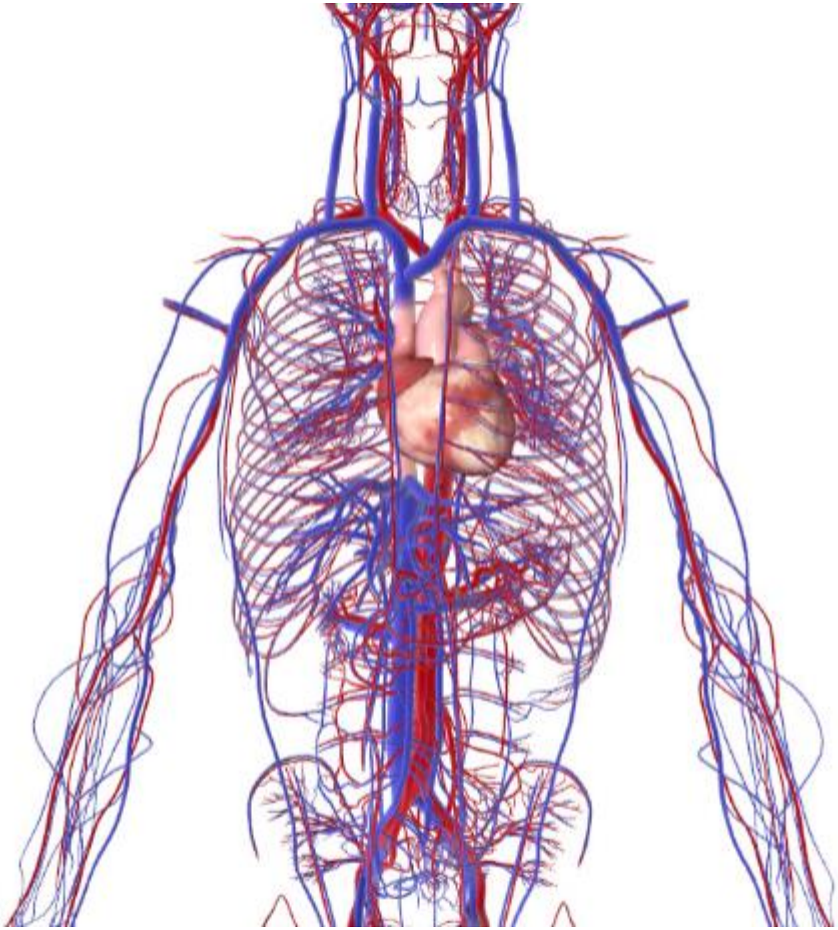
Διδάσκων:

Michael Neidlin

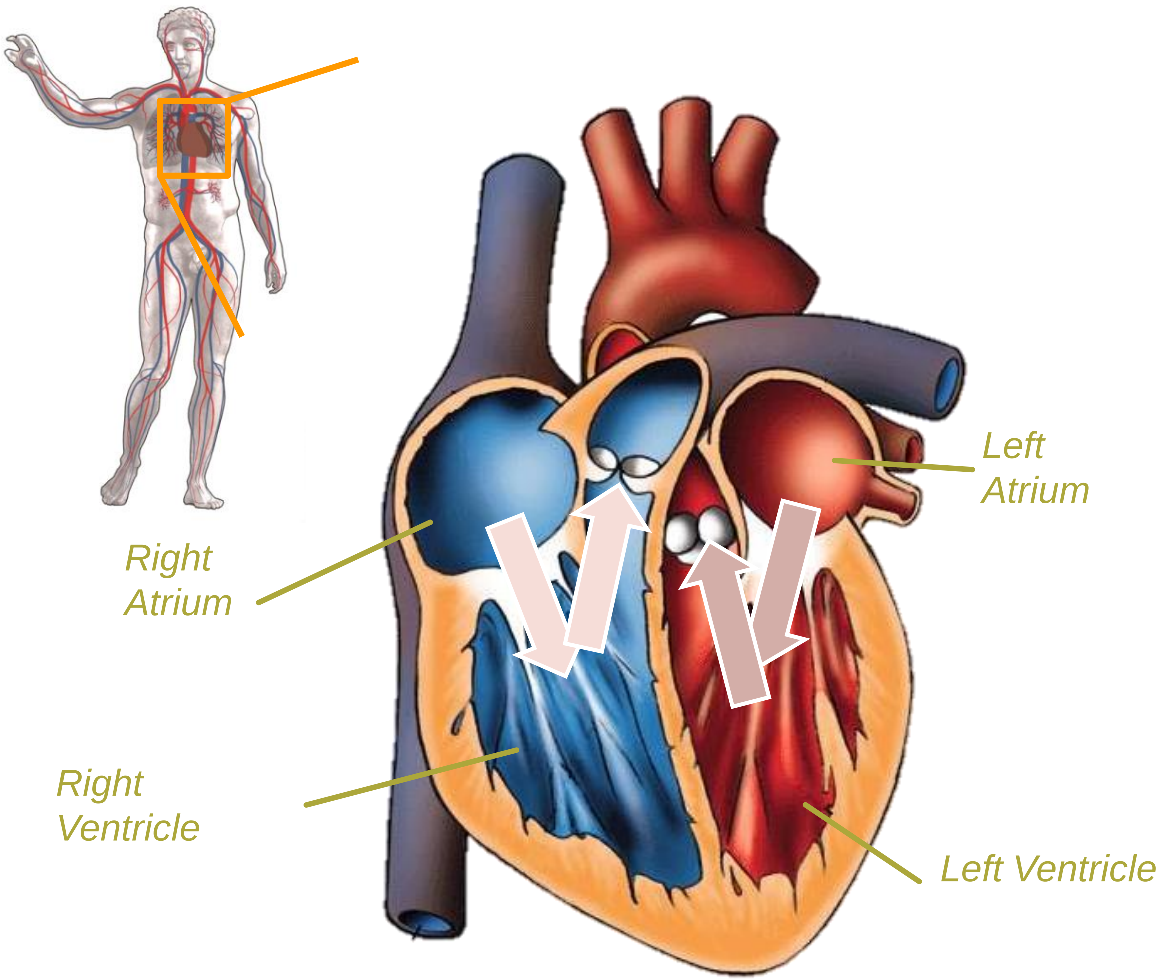
Content

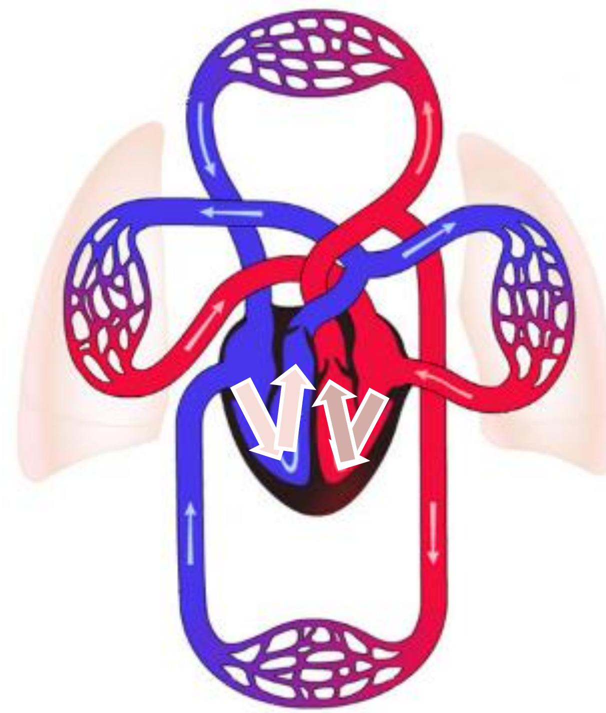
- Cardiovascular System/Respiratory System/Renal System
  - Anatomy
  - Physiology and Mechanics
  - Pathologies and Therapies (Devices)

Cardiovascular System

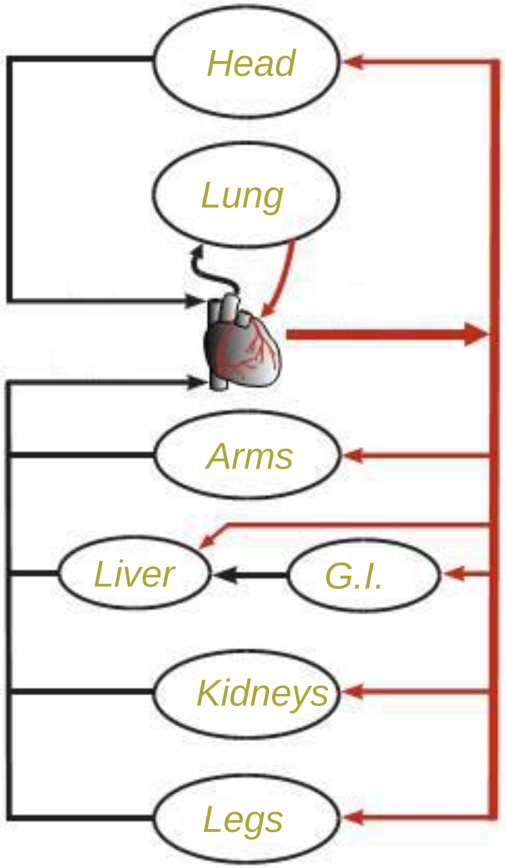


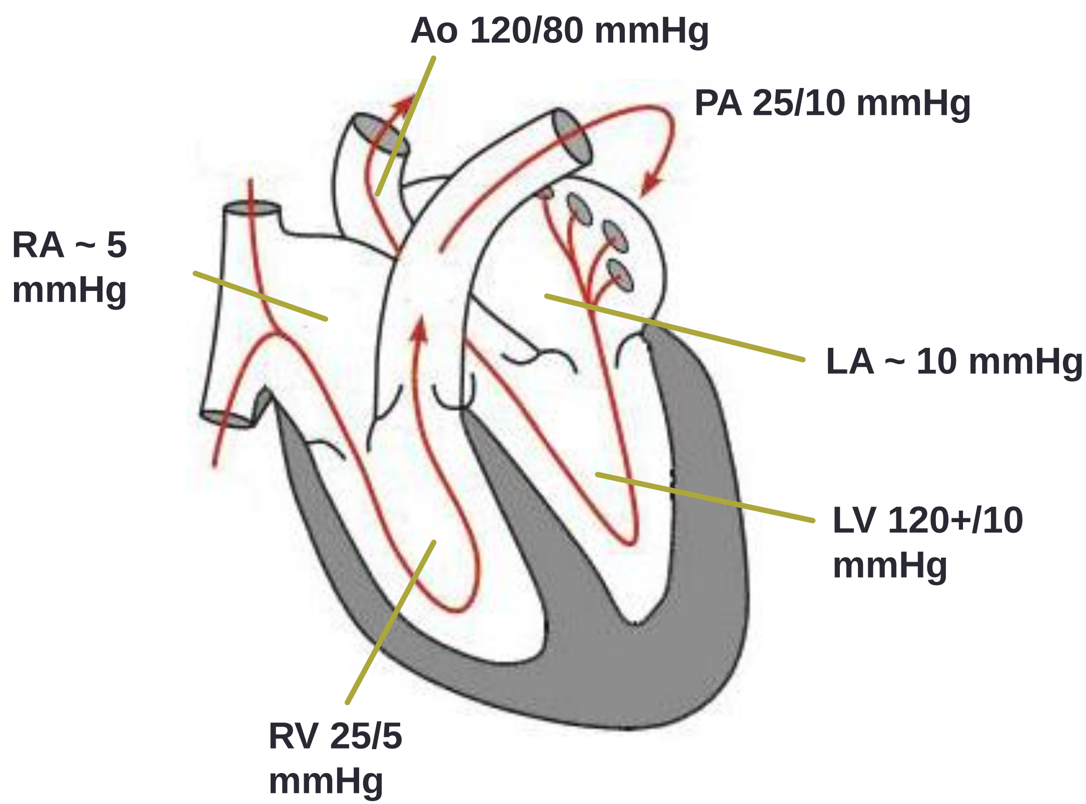
Anatomy and Physiology





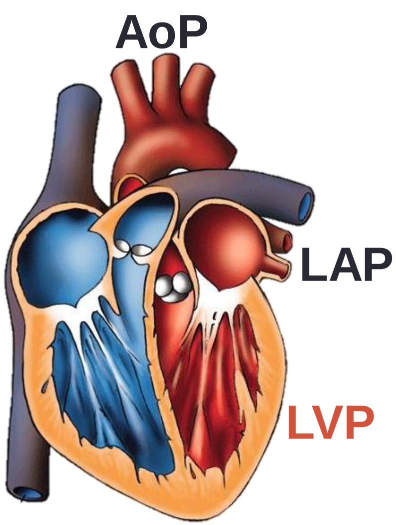
Pressures

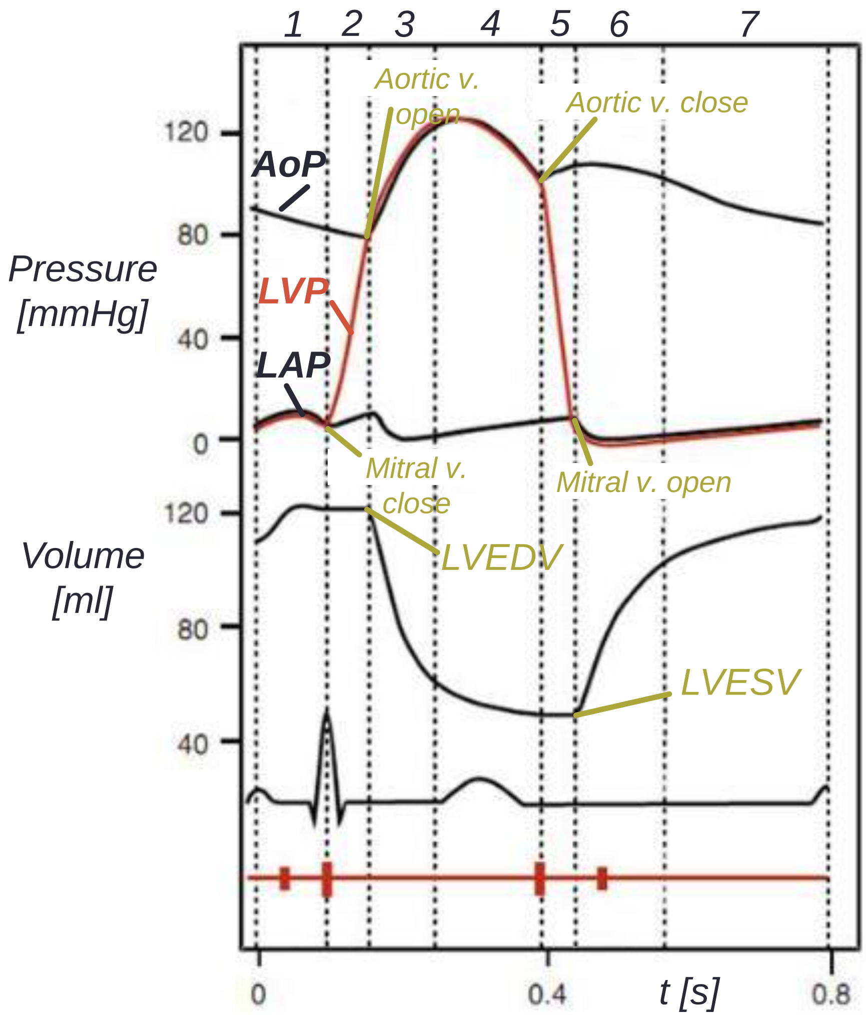

Head
Lung
Arms
Liver
G.I.
Kidneys
Legs


Ao 120/80 mmHg
PA 25/10 mmHg
RA ~ 5 mmHg
LA ~ 10 mmHg
LV 120+/10 mmHg
RV 25/5 mmHg

Cardiac Cycle of the LV

- 7 Phases
  - (1) Atrial Systole
  - (2) Isovolumetric contraction
  - (3) Quick ejection
  - (4) Reduced ejection
  - (5) Isovolumetric relaxation
  - (6) Quick filling
  - (7) Reduced filling





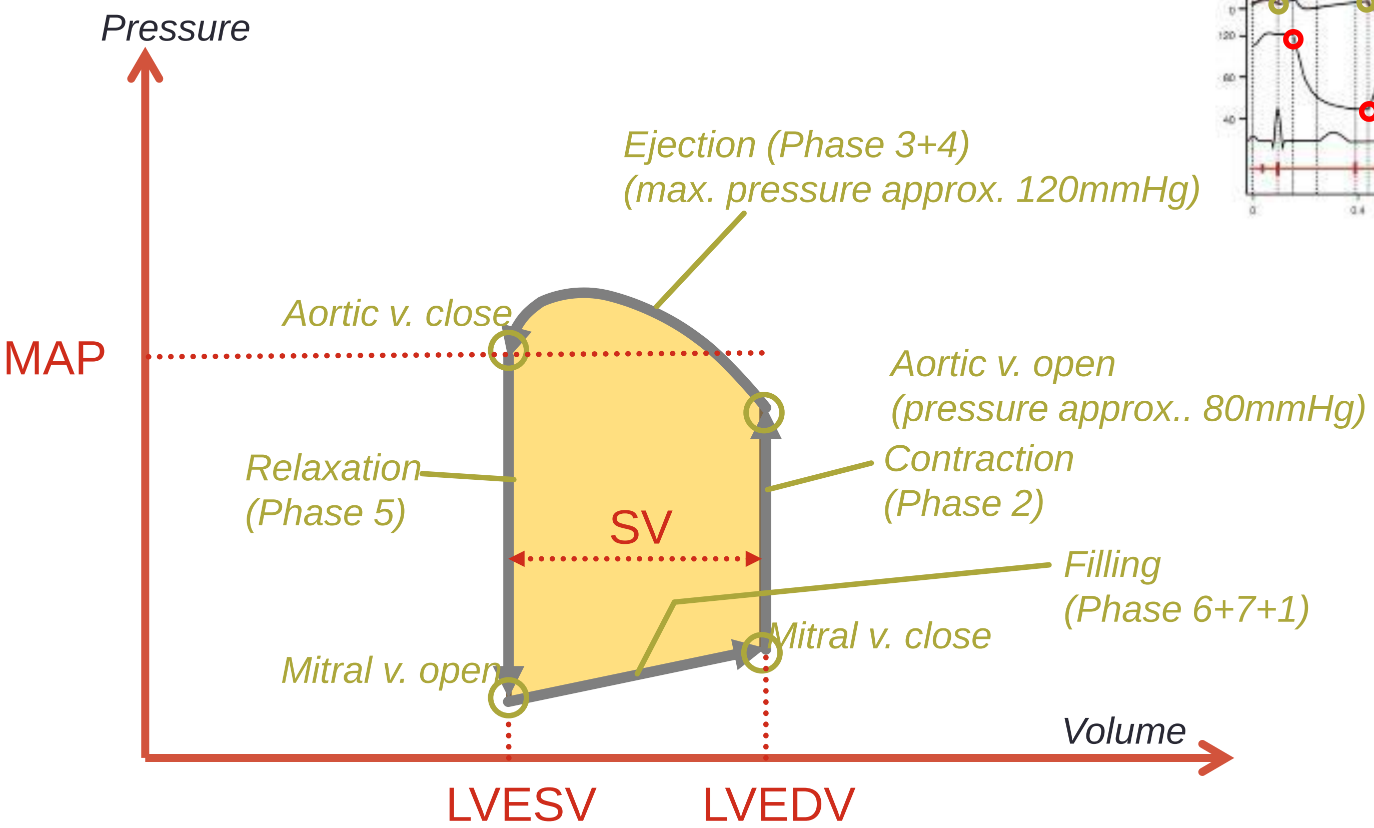
Beating Heart Animation

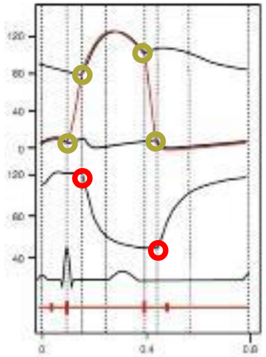
https://www.youtube.com/watch?v=0NmWOHuy-o8

Nomenclature

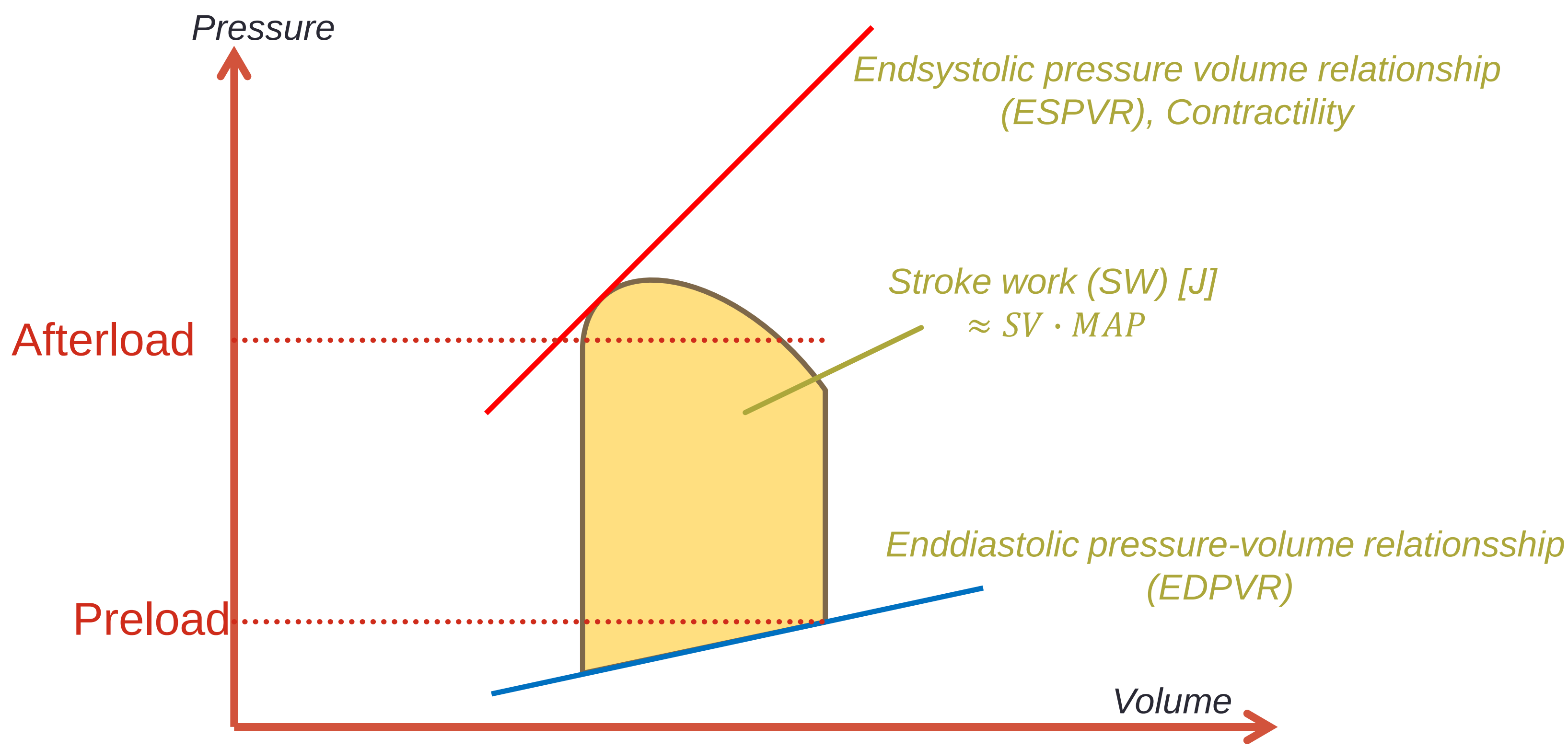
- CO : Cardiac Output (4.9 l/min)
- HR : Heart Rate (70 / min)
- SV : Stroke Volume (70 ml)
- ESV/EDV : Endsystolic/Enddiastolic Volume (50ml/120ml)
- EF : Ejection Fraction $EF = \frac{SV}{EDV} \cdot 100 = \frac{EDV - ESV}{EDV} \cdot 100 \ [\%]$
- Healthy EF 60%, Heart Failure EF <30%

Pressure-Volume Diagram (PV-Loop)



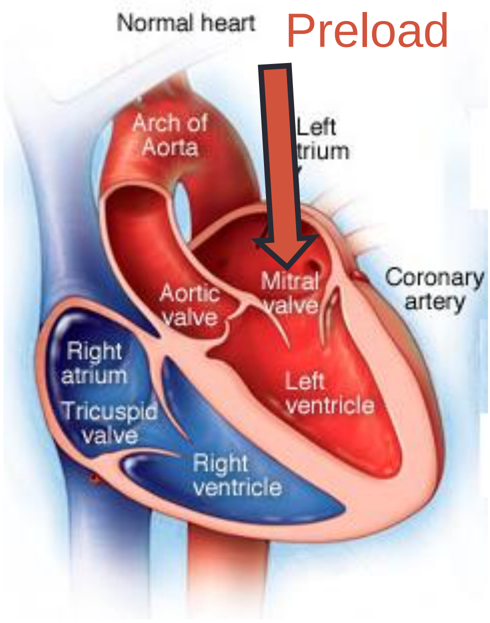


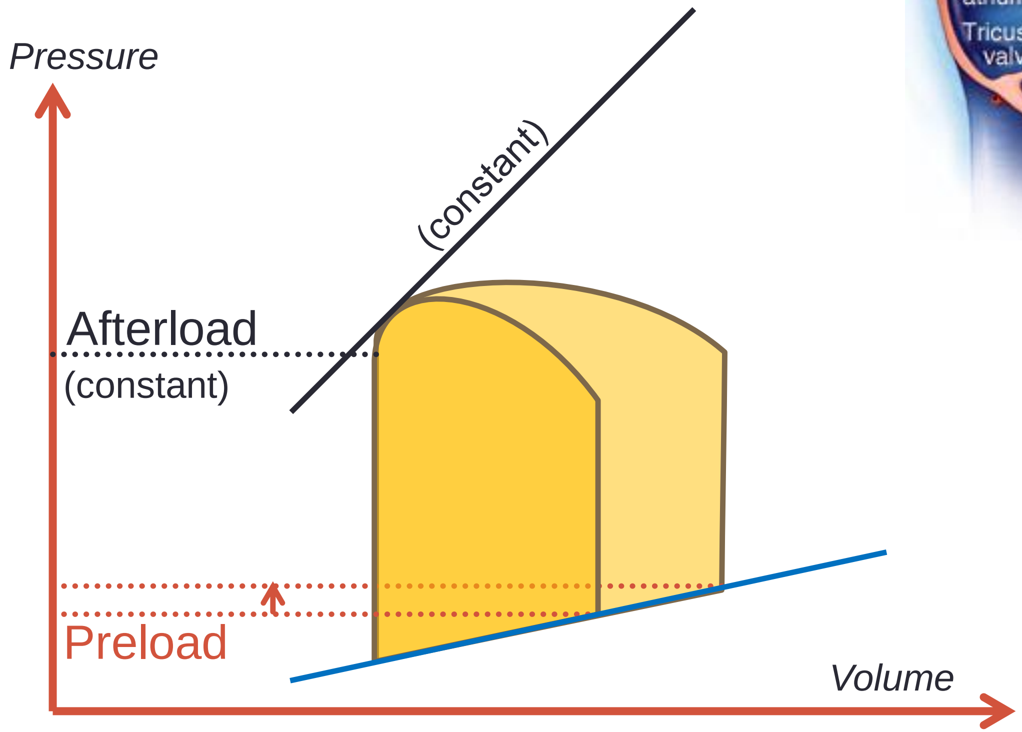
PV-Loop


Pressure
Endsystolic pressure volume relationship
(ESPVR), Contractility
Stroke work (SW) [J]
$\approx SV \cdot MAP$
Afterload
Enddiastolic pressure-volume relationsship
(EDPVR)
Preload
Volume

Changes of PV-Loop

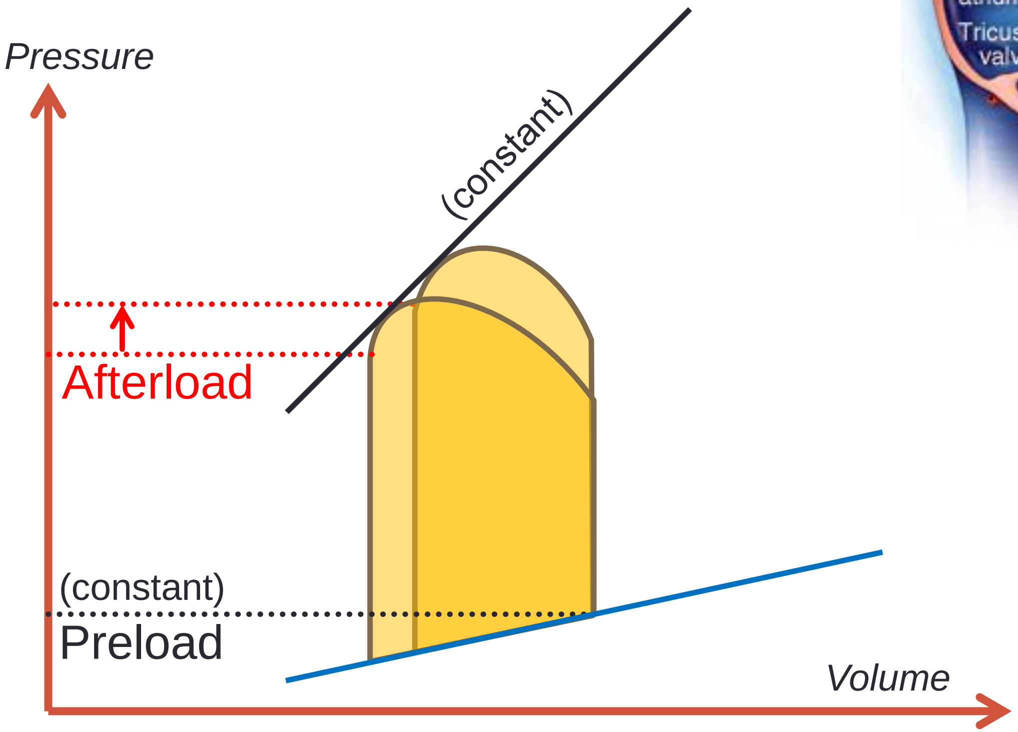
- Increased preload
  - Increased systolic pressure
  - Increased stroke volume

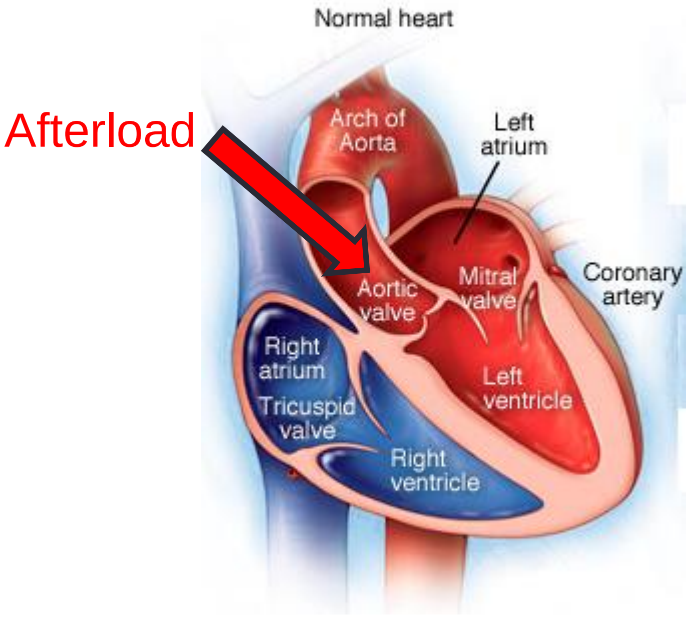




Changes of PV-Loop

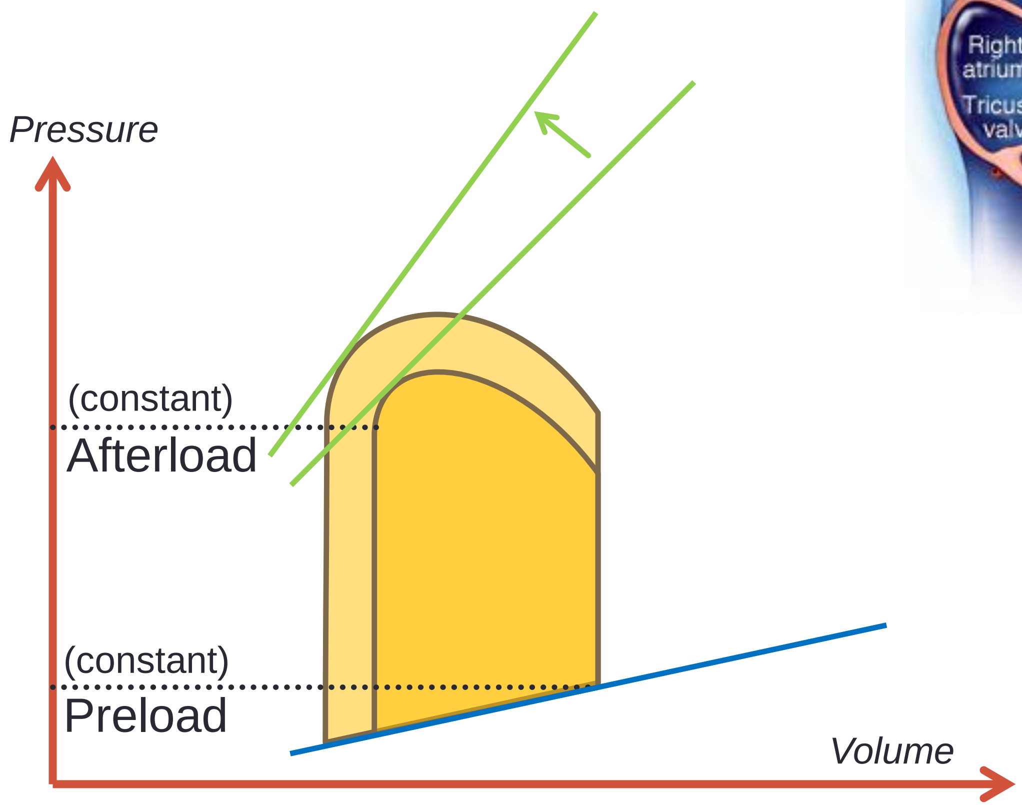
- Increased afterload
  - Increased systolic pressure
  - Decreased stroke volume

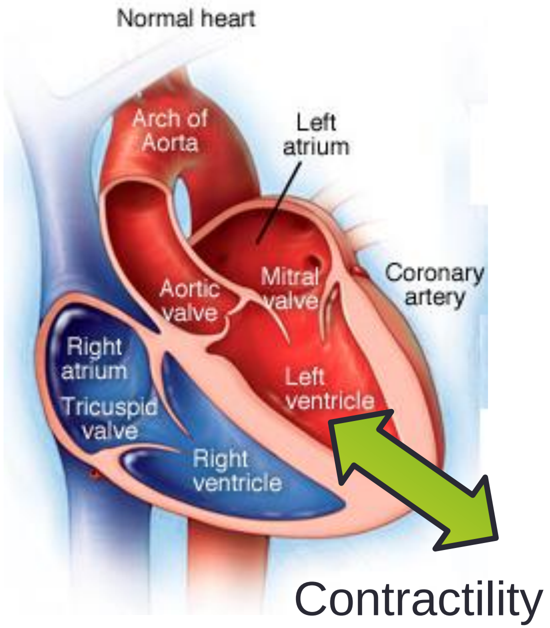




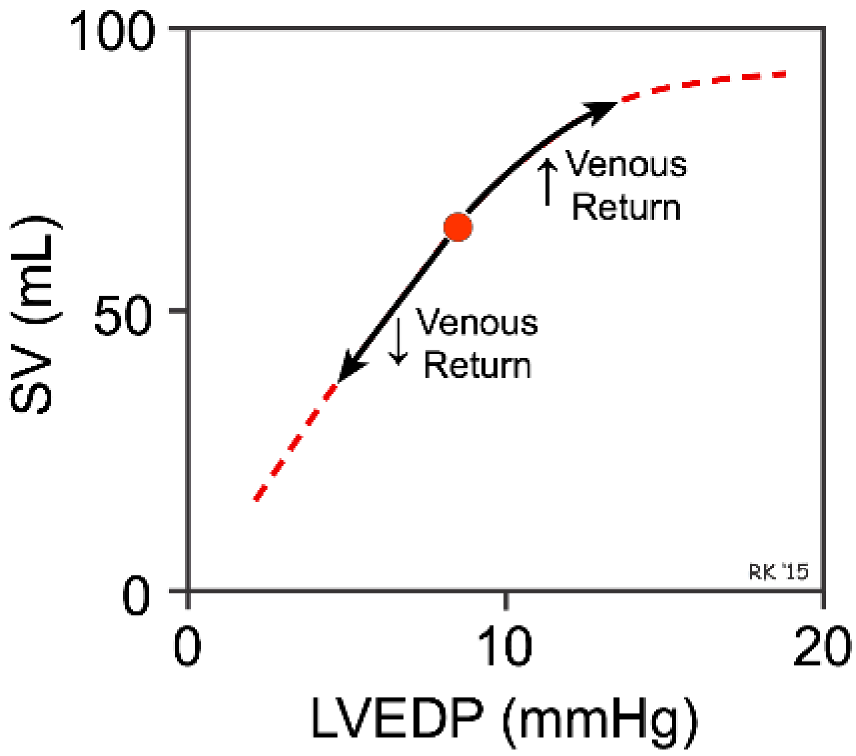
Changes of PV-Loop

- Increased contractility
  - Increased systolic pressure
  - Increased stroke volume





Frank-Starling Law



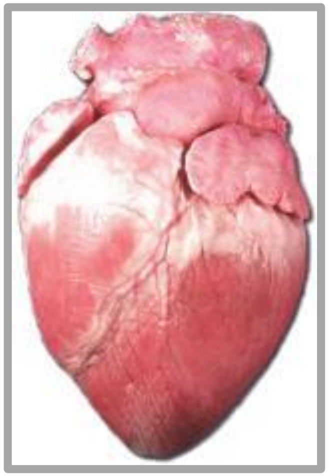
Ability of the heart to change its force of contraction and therefore stroke volume in response to changes in venous return

Summary

- Heart is a 4 chamber pump with 4 passive valves
- LV and RV eject the blood through the entire CVS to the RA and LA respectively
- Preload, Afterload and Contractility describe the performance of the heart
- PV Loop for visualization
- Ventricle adapts to system state (Frank-Starling Law)

Questions?

Heart dynamics



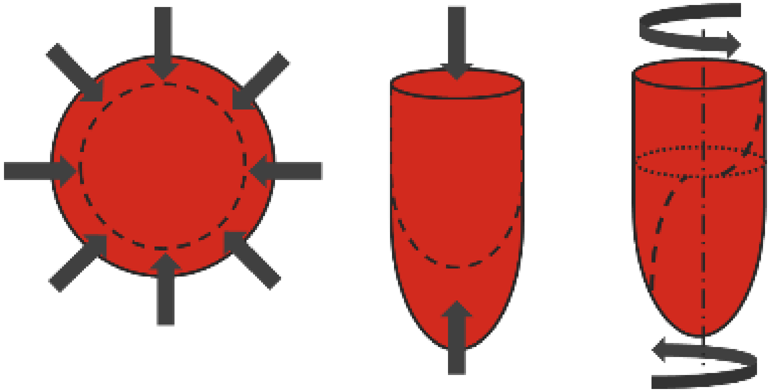
Durability [Years]	79,68	10
Hours	698.000	5.000
Cycles / Turnarounds	3 Bio.	1 Bio.

Pumped blood volume: 210000000 L

Why is the heart so efficient?

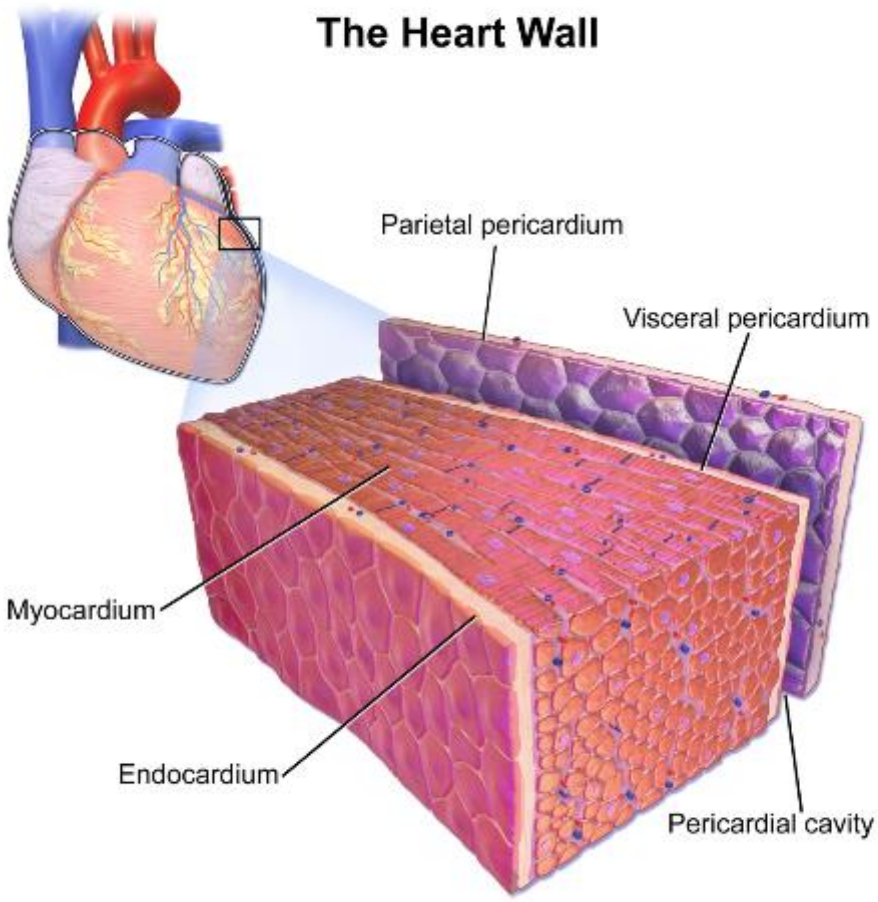
Ventricular contraction – Superposition of three movements

https://www.youtube.com/watch?v=oHMmtqKgs50

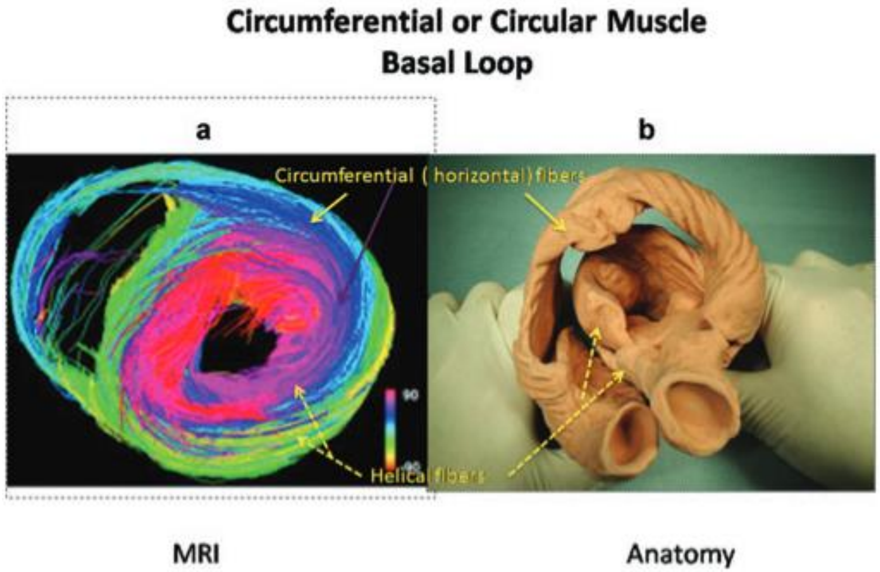


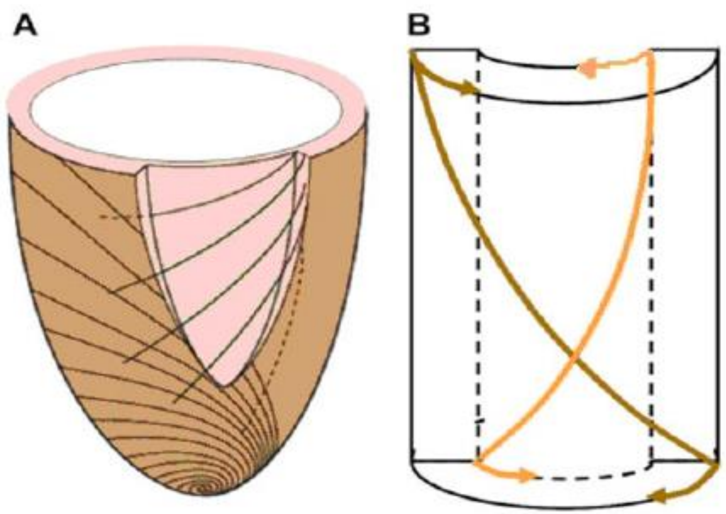
www.youtube.com

Structure of the cardiac muscle

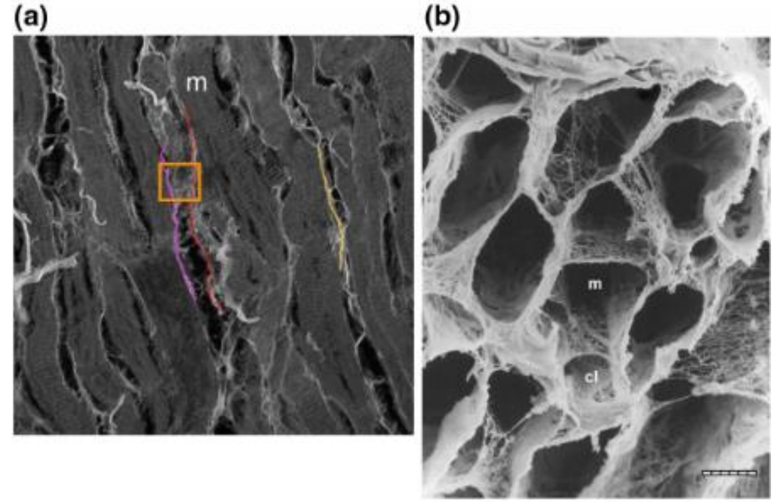


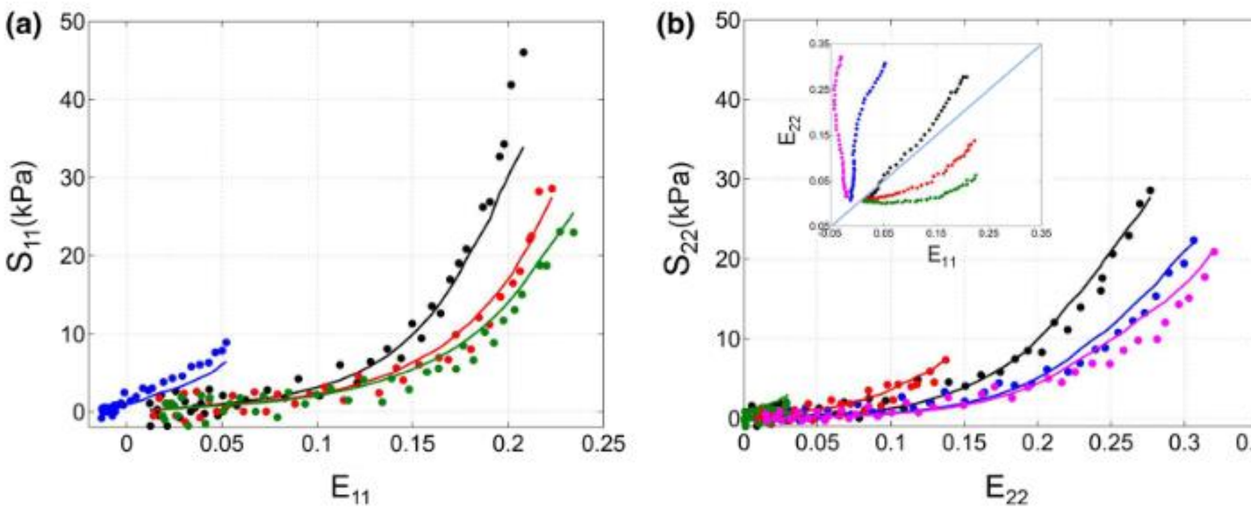
Orientation of myocardial fibres





In vivo material properties of myocardium





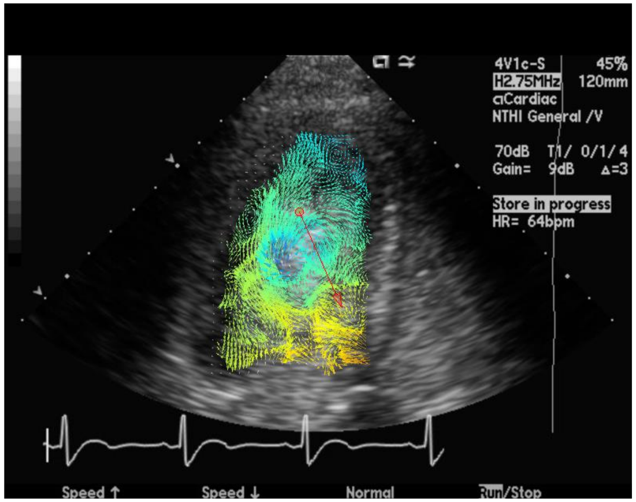
L3 Soft tissue material properties

Myocardial tissue is **hyperelastic** and **fiber-reinforced** (anisotropic) material

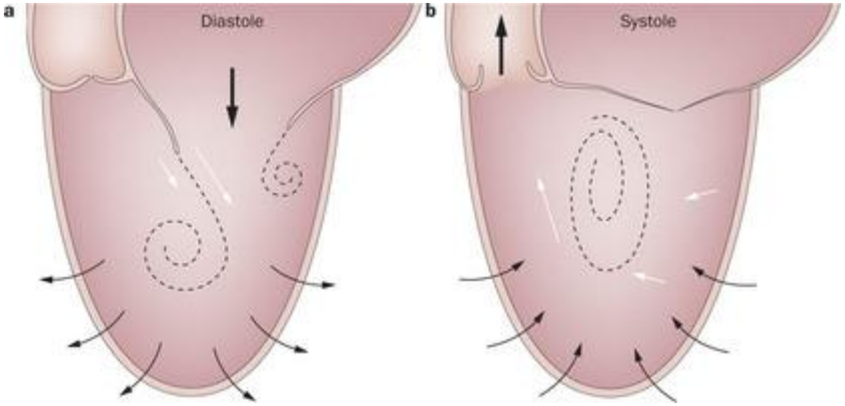
Flow structures define cardiac health

www.apotheken-umschau.de

https://www.youtube.com/watch?v=MHaWwa0JNbw

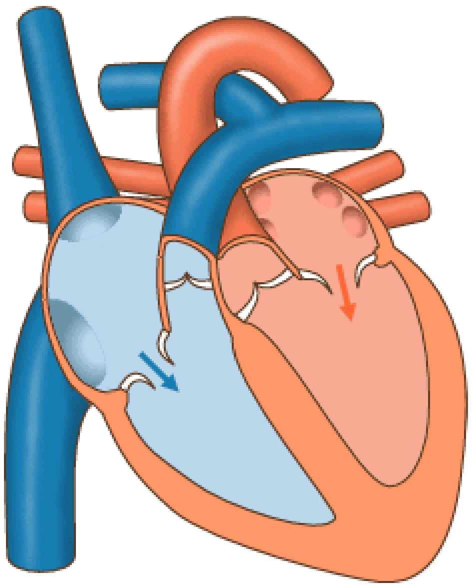


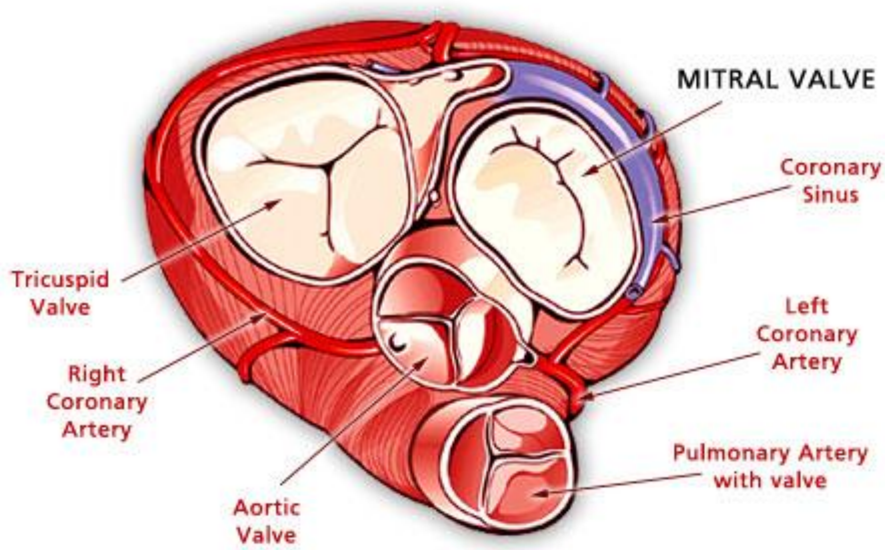
Healthy ventricle Diseased ventricle



Pedrizzetti, Gianni, et al. "The vortex - an early predictor of cardiovascular outcome?." *Nature Reviews Cardiology* 11.9 (2014): 545-553.

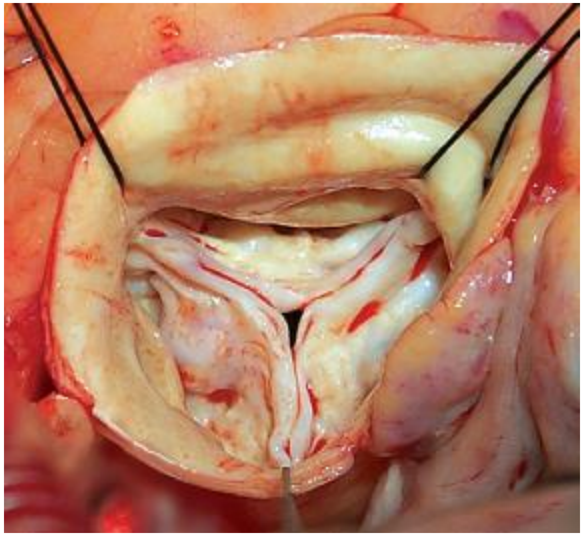
Heart valves





Properties:
- Passive opening
- Tightness against backflow
- Very low pressure drop across valve (<1 mmHg)

Heart Valve replacement



The perfect machine

Lifelong durability

Vortex structures for energy conservation

https://www.youtube.com/watch?v=DeOgt4kP2Ys

Optimized efficiency

Turbulent mixing of oxygen and nutrients

Big operation range
60-210 mmHg
3-30 l/min

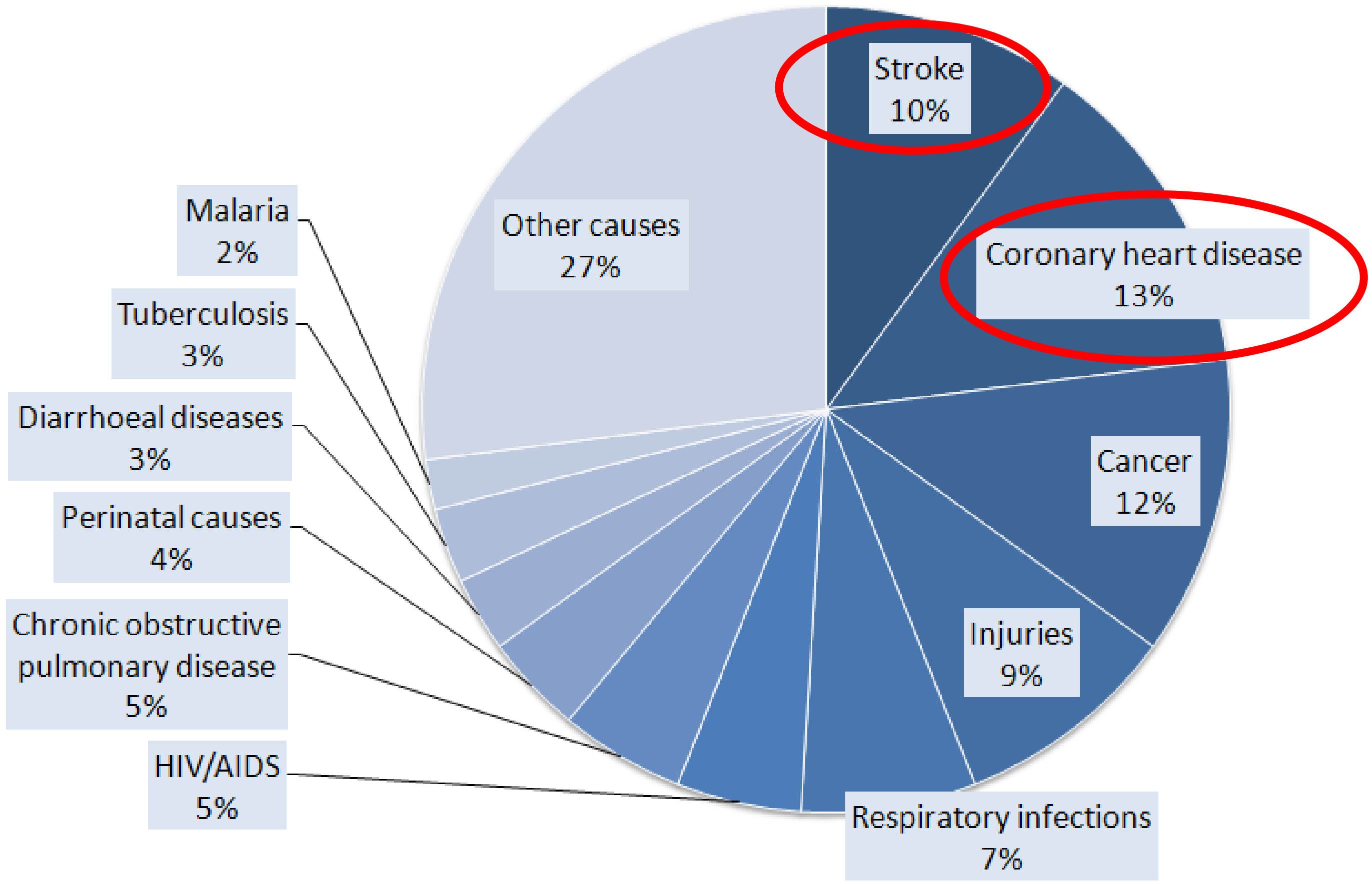
Questions?

The heart and cardiovascular system

- Function and system analysis ✓
- Mechanical structure and of the heart ✓
- Influence on hemodynamics ✓
- Heart valves ✓

- Pathologies
- Therapy and Examples

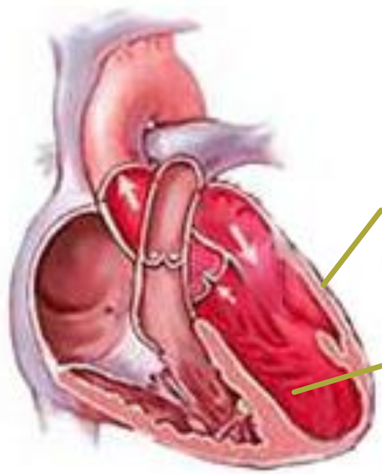
The Top "Killers" in 2004



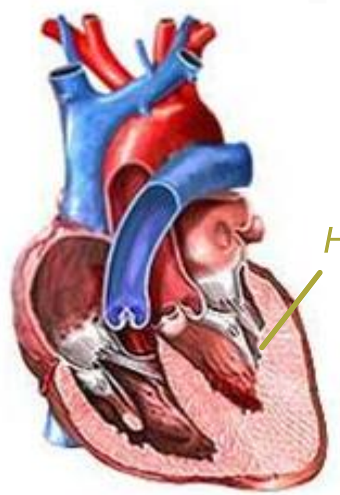
=> In 2004, more than 29 % of all deaths were related to cardiovascular diseases

Source: World Health Organization WHO – N°310 (updated 2008)

Pathologies

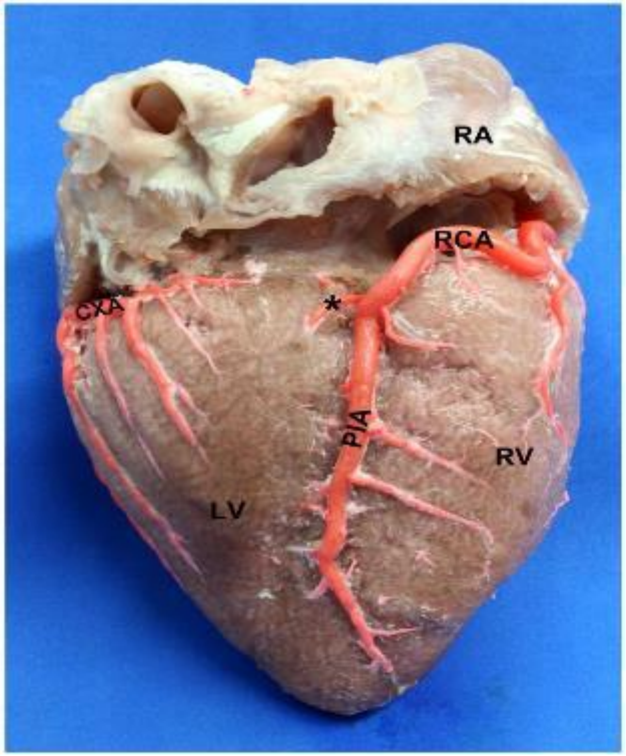


Dilatative cardiomyopathy



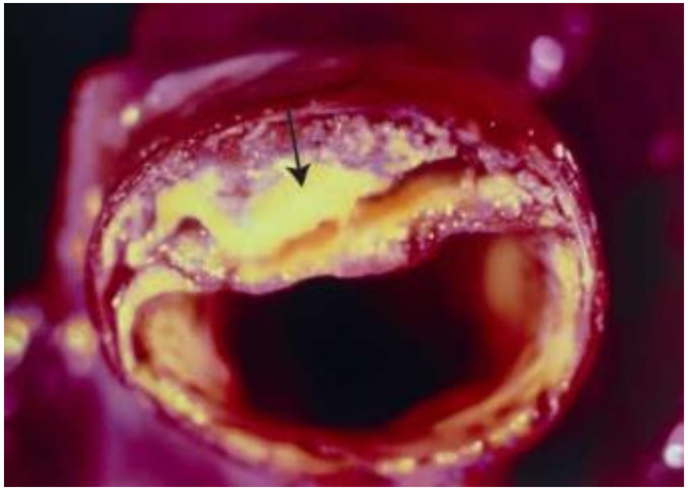
Hypertrophic cardiomyopathy

Coronary Heart Disease (CHD)



Most common cardiovascular disease

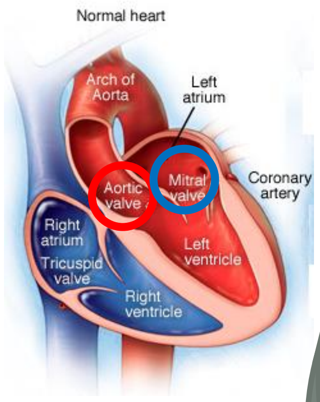
Stenosis of coronary arteries (atherosclerosis)
Reduces myocardial blood flow and leads to
Ischemia of heart muscle



Understand the mechanics of CHD

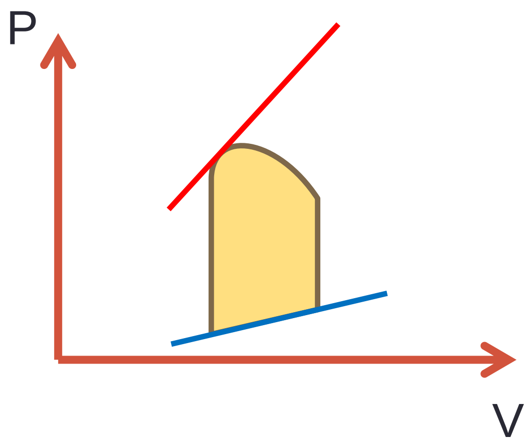
Unhealthy life style (fat, sugar, cigarettes, little physical activity, stress)
[of course genetic and congenital factors also play a role!]

Arterial stenosis and high blood pressure



Afterload increase

Higher LV pressures necessary



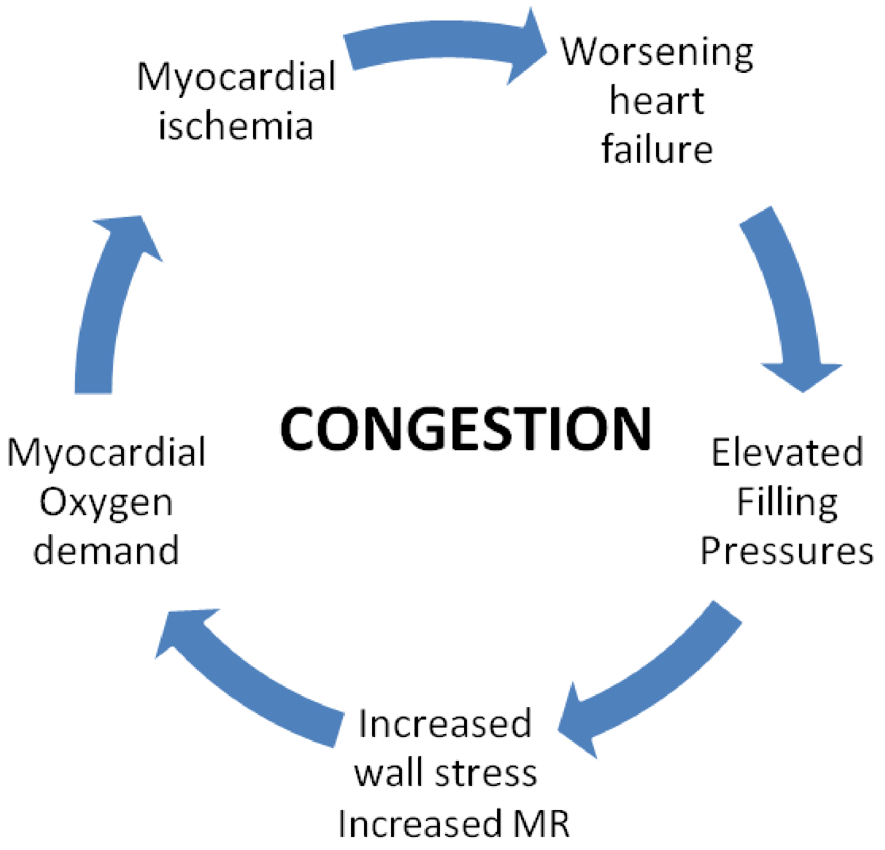
Preload increase

High Myocardial stress & High Oxygen and Blood demand

HEART FAILURE – High preload, low/no CO, low afterload

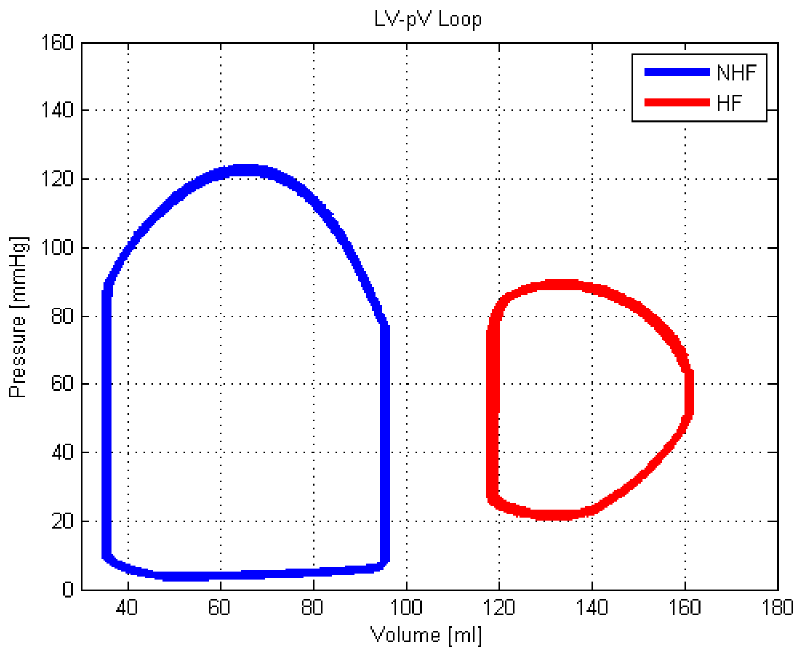
Clinical Perspective

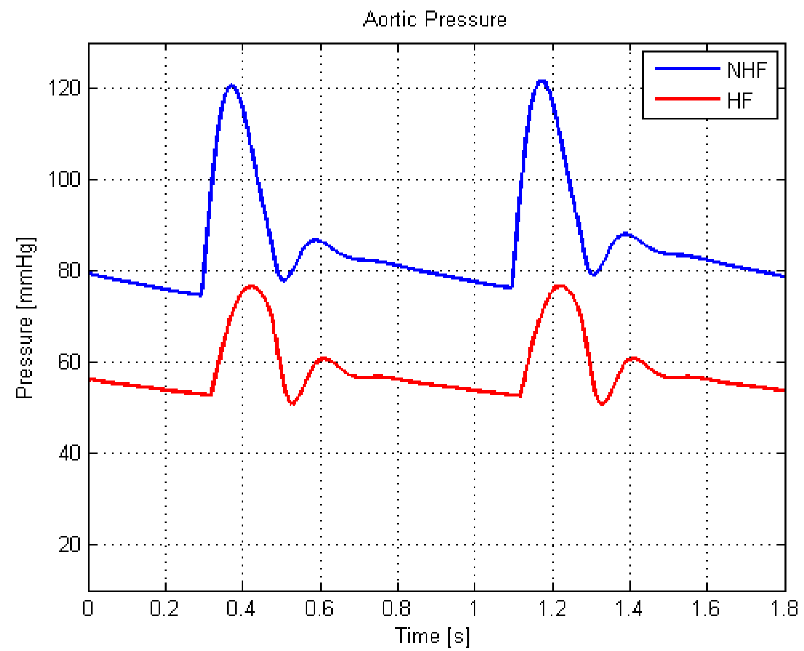
Vicious Cycle of Congestion in Acute Heart Failure

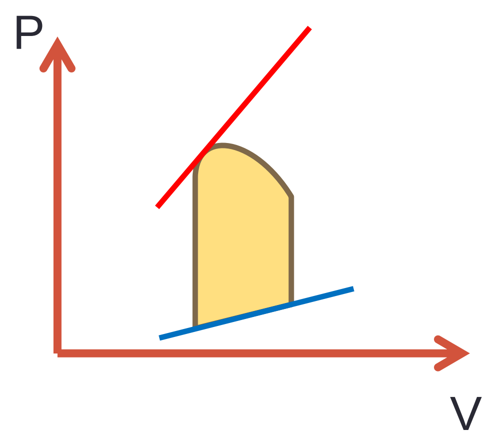


Deduce a therapy option from engineering point of view

HEART FAILURE – High preload, low afterload, low/no CO







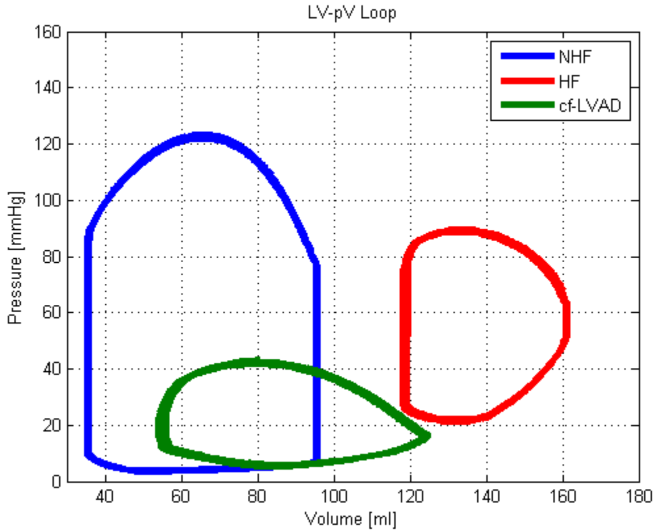
Ventricular Assist Device for End-Stage-Heart Failure

Continuous flow pump that bypasses the aortic valve and unloads the LV

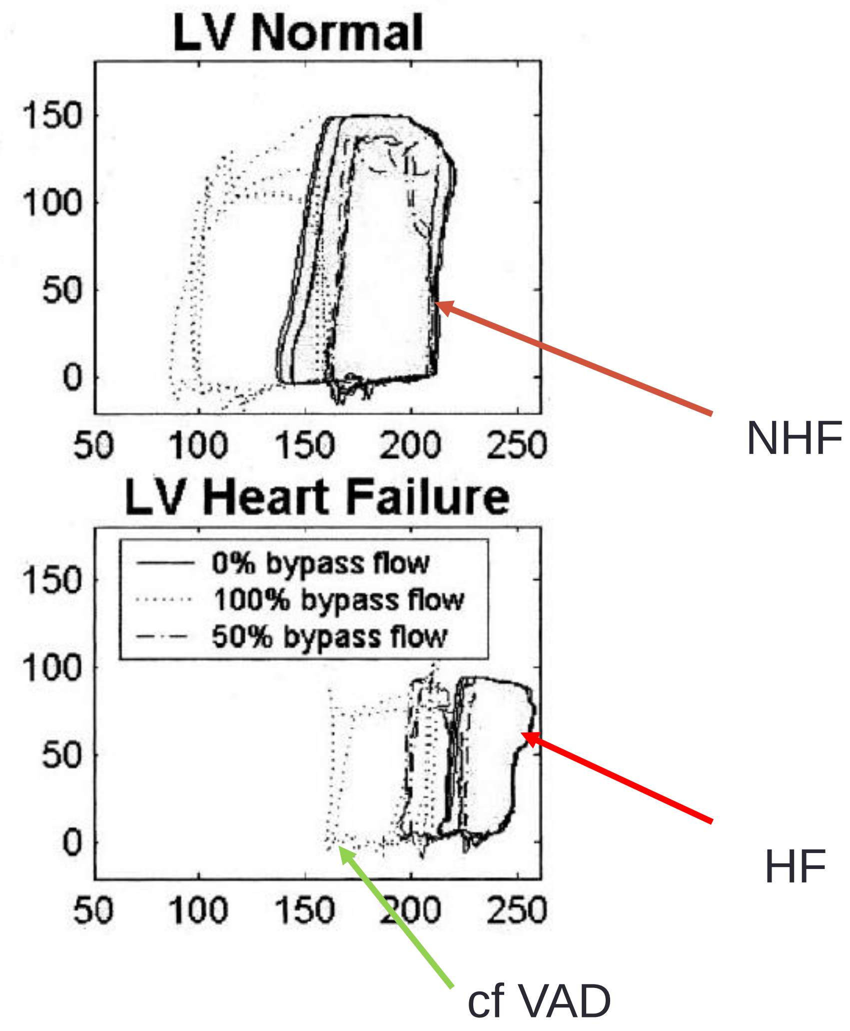
LV pressure reduction, SV increase

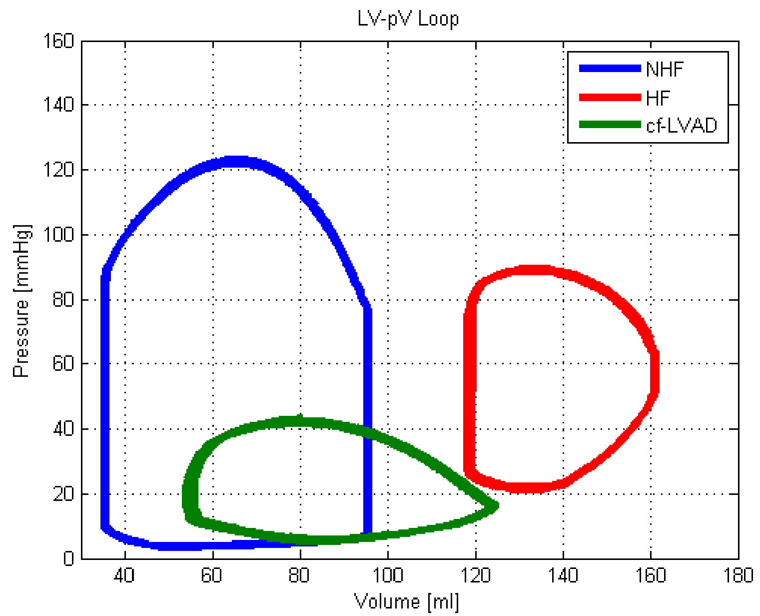
Preload reduction

Afterload reduction



Results from in vivo animal trials





Heartmate II surgery

- https://www.youtube.com/watch?v=I4r5_3uS0Nc&t=658s

Examples of Current Devices

Berlin Heart Incor

HeartWare HVAD

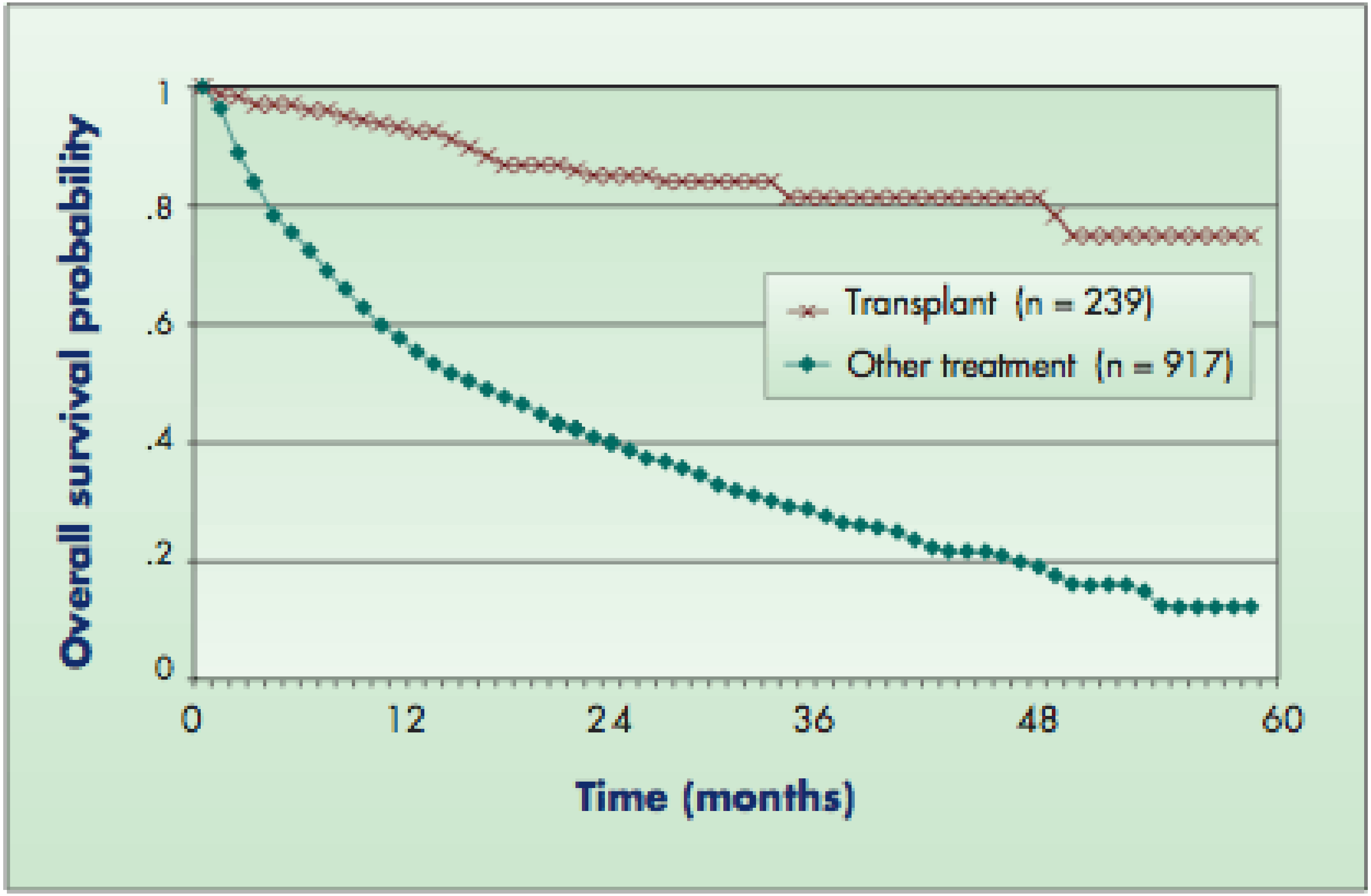
Terumo DuraHeart

Levacor

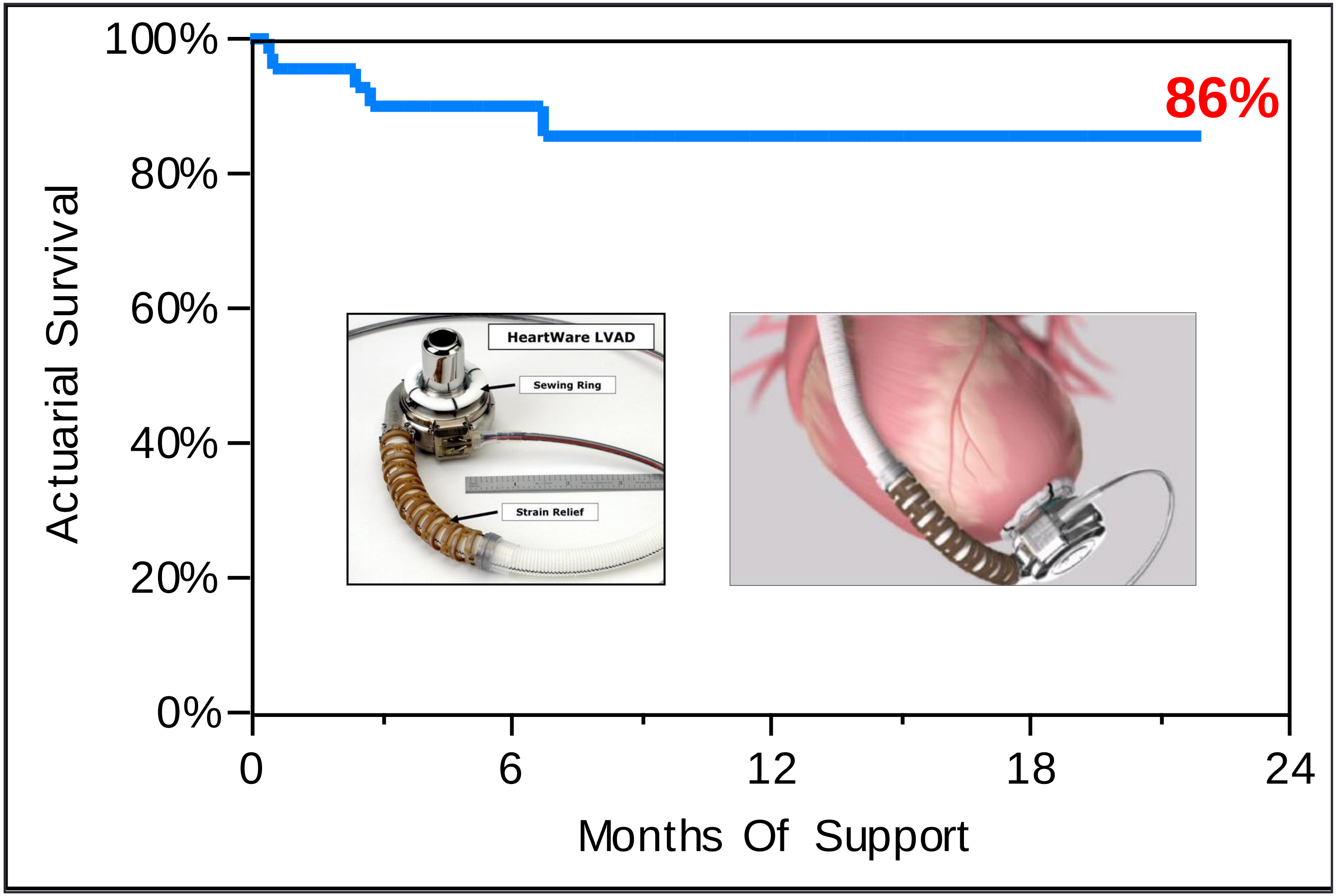
Heartmate II

MiTiHeart

Transplant is the gold standard (until now)



But the engineers are getting there



=> Survival rate on newest cardiac assist devices compares to heart transplant

VAD success stories

By courtesy of **Prof. H Schima**
Center for Biomedical Eng. & Physics, Dept. for Cardiac Surgery
Research Group on Cardiovascular Dynamics and Artificial Organs

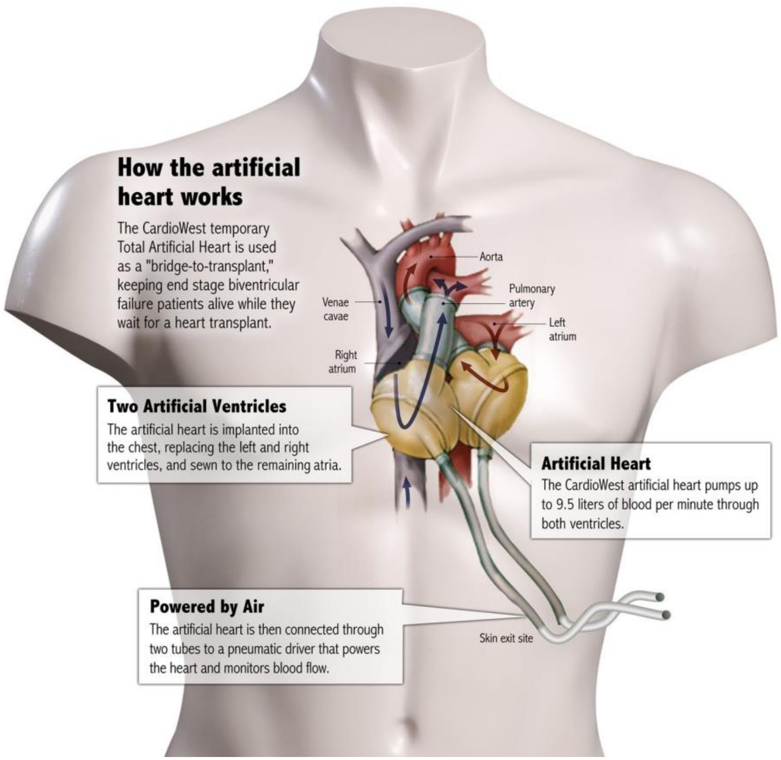
Total Artificial Heart : 2x Heartmate

10.3.2011: Implantation of 2 continuous flow pumps

NO HEARTBEAT AT ALL !

Syncardia TAH

Principle:



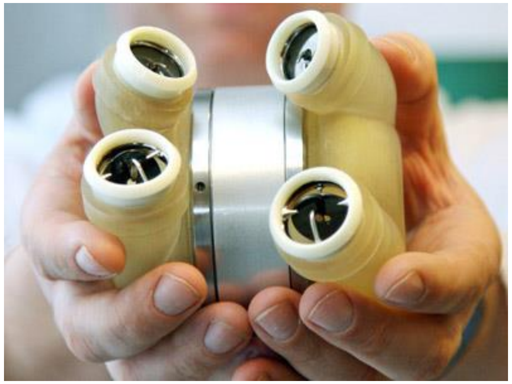
Pneumatic Drive

>1200 Implants since 1993

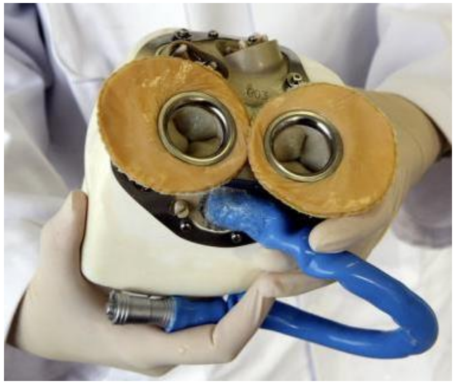
“Bridge-to-transplant”, max. time 4 years

TAH: Current developments

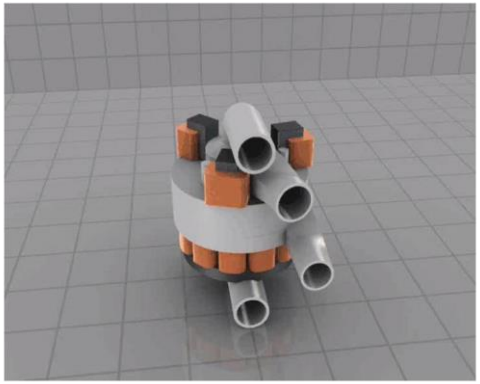
MagScrew



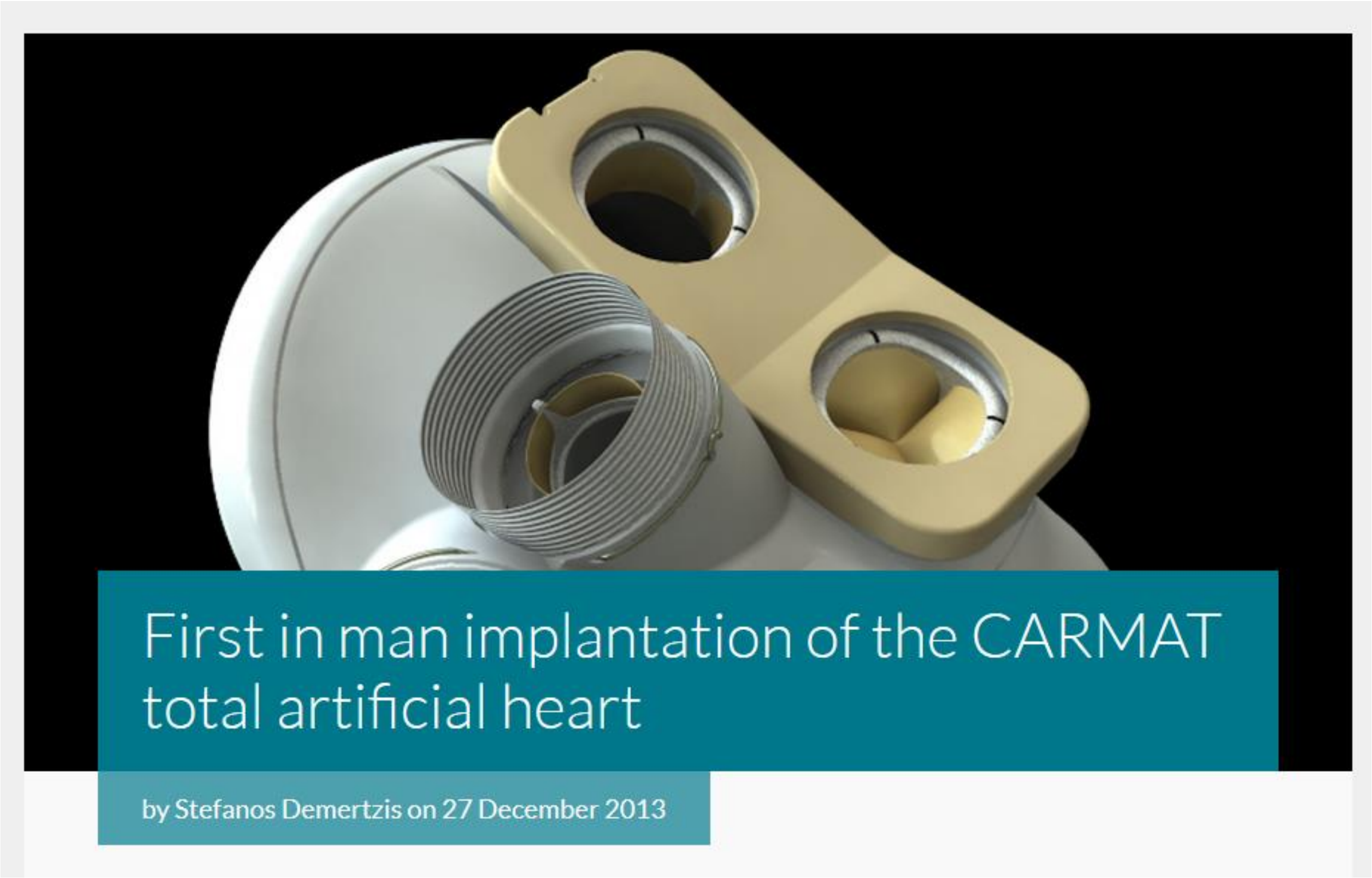
ReinHeart



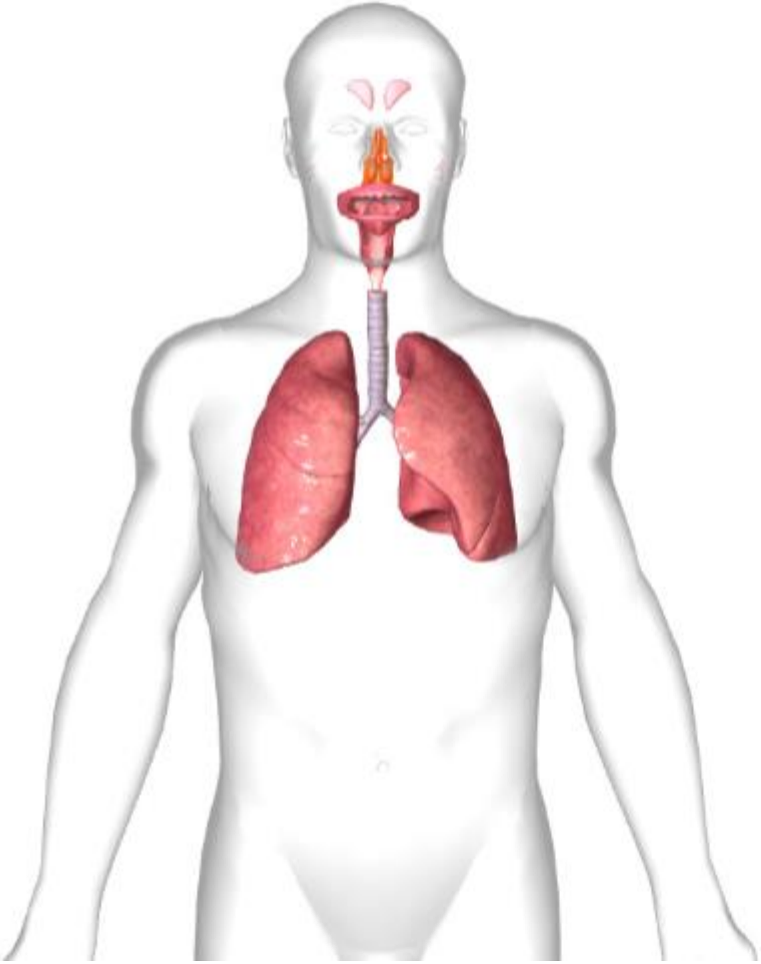
CARMAT



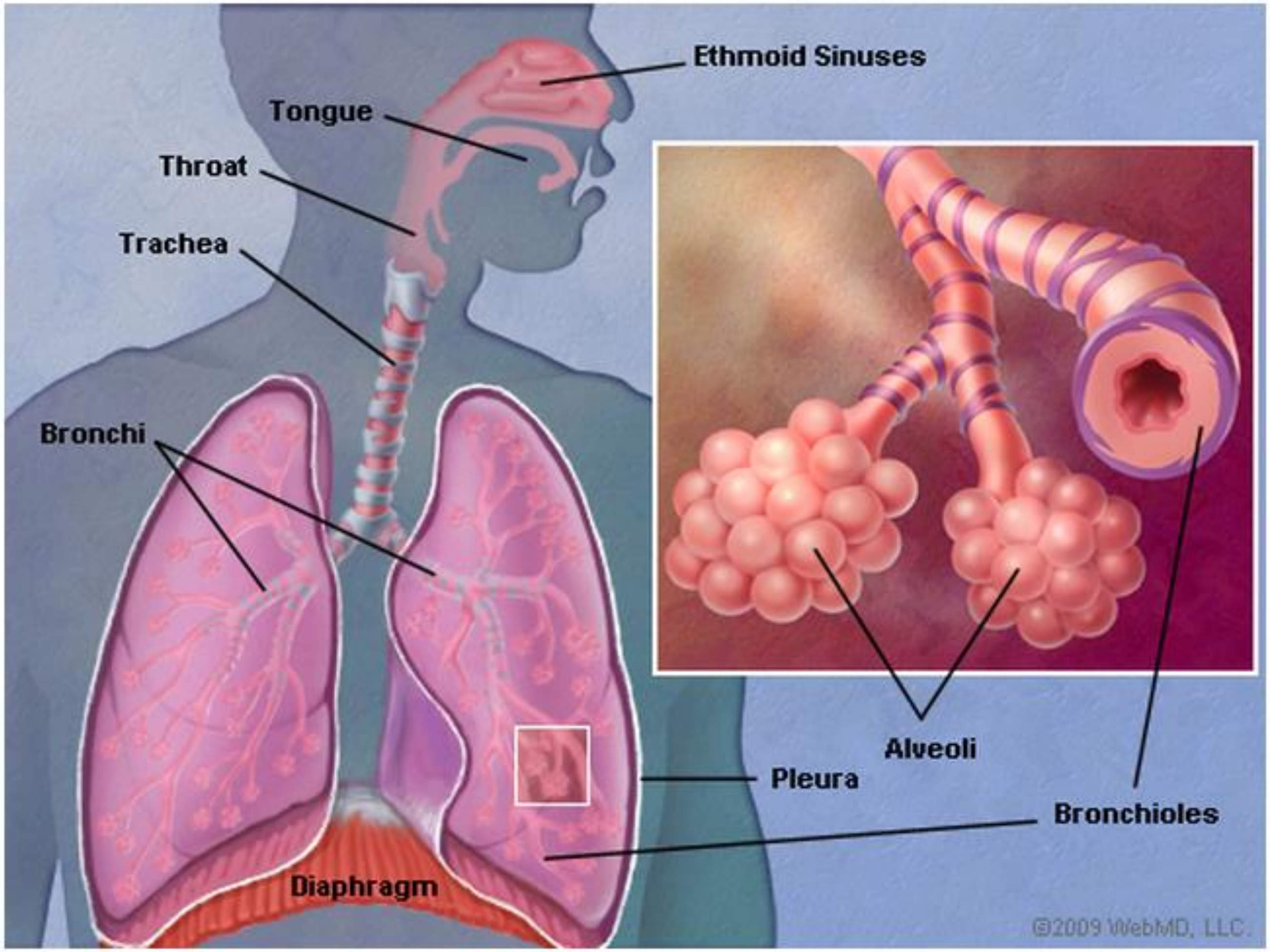
BiVACOR


First in man implantation of the CARMAT total artificial heart
by Stefanos Demertzis on 27 December 2013

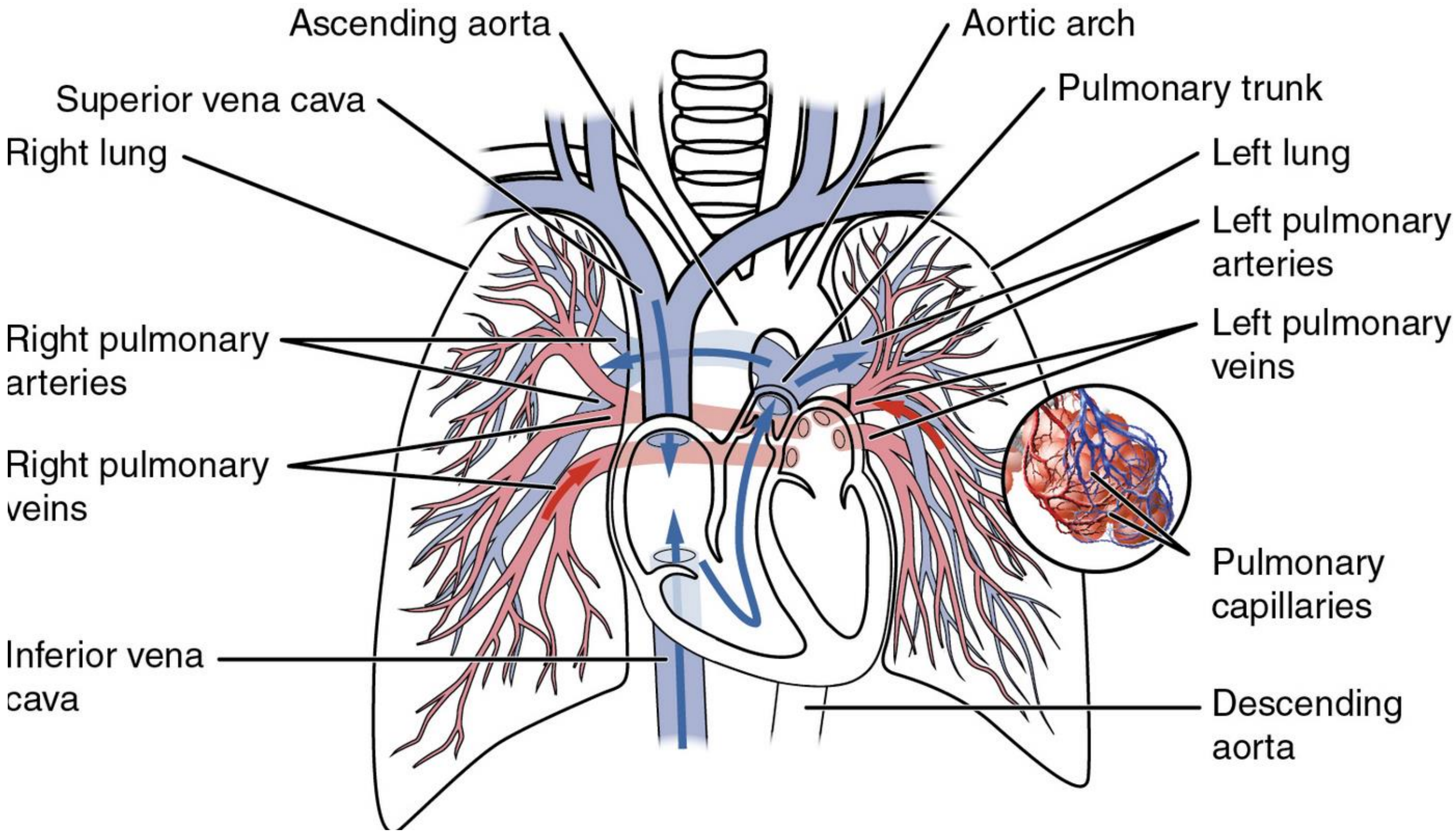
Respiratory System



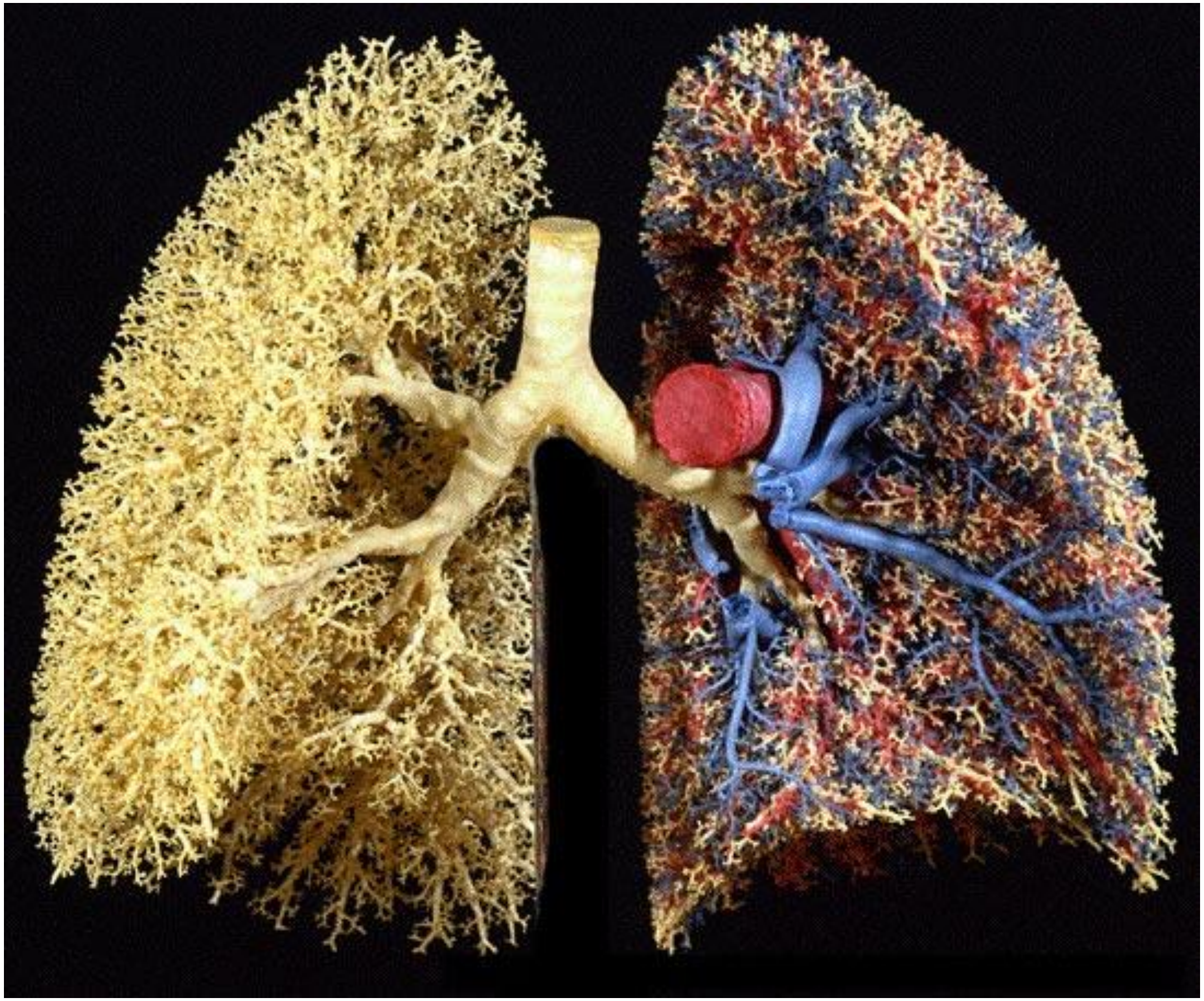
Anatomy and Physiology



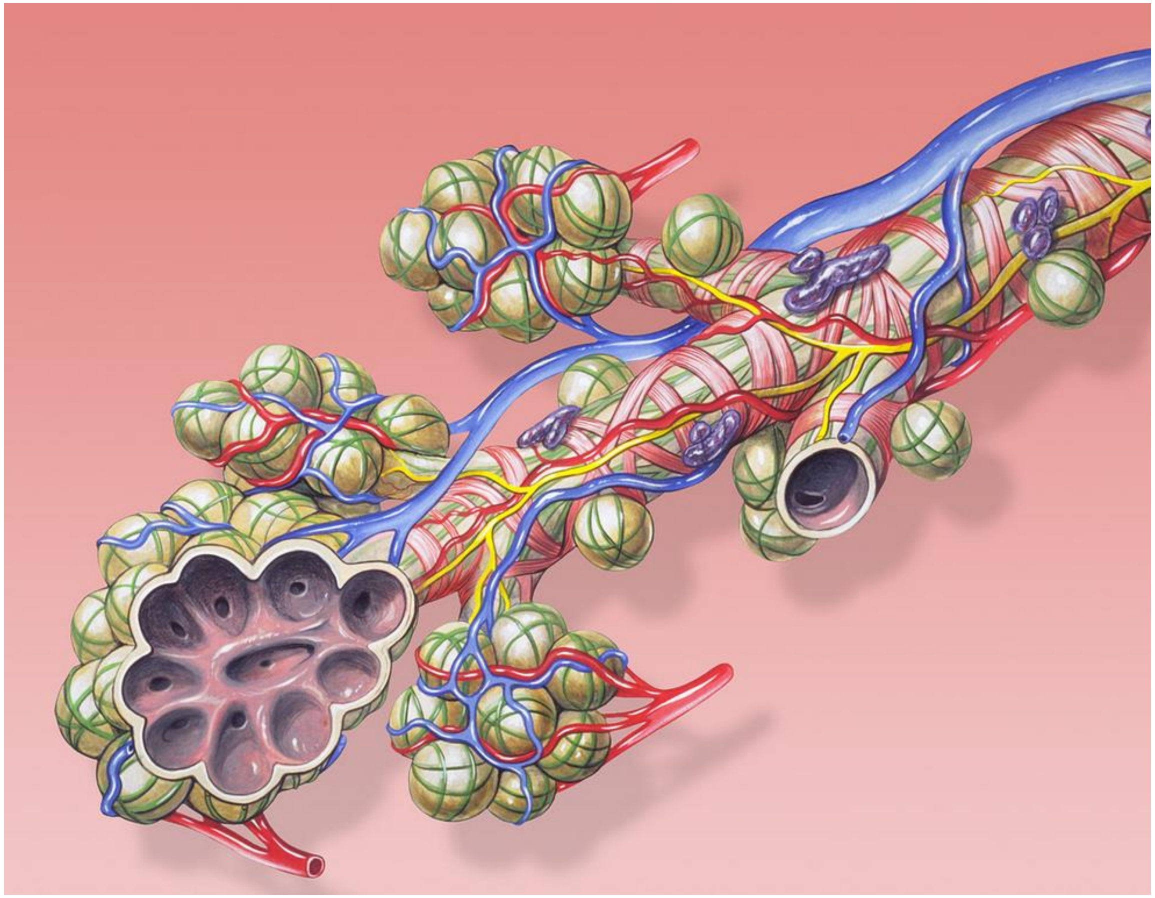
Blood supply



Airway system and blood supply cast

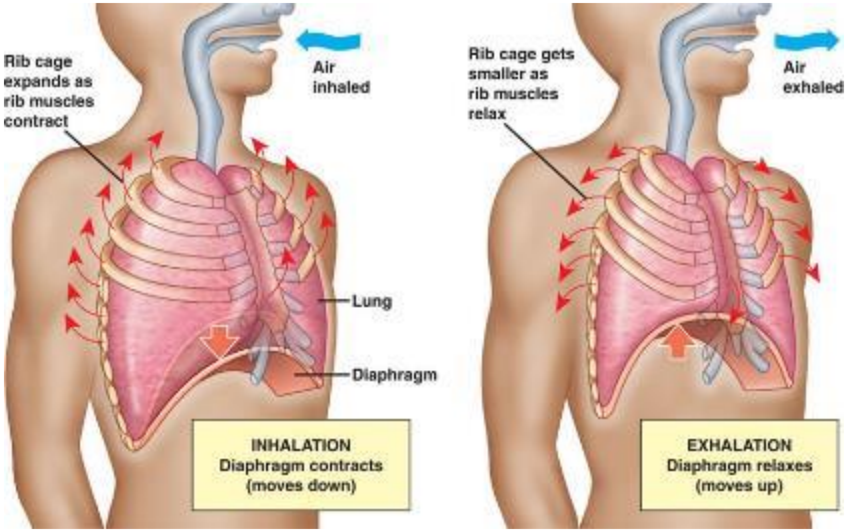


Alveoli



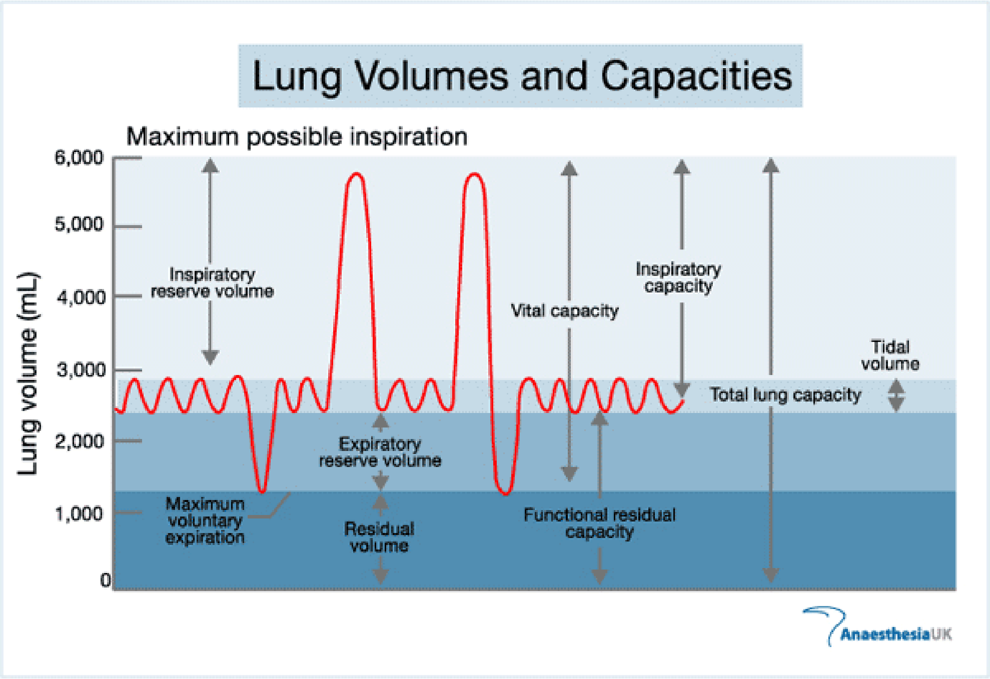
About 700 million alveoli with total area of 75 m^2

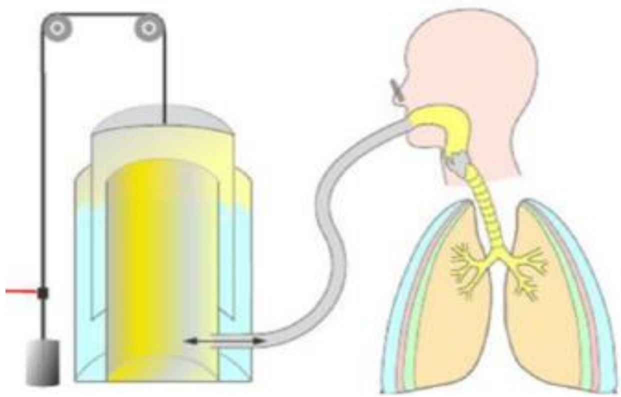
How do we breathe

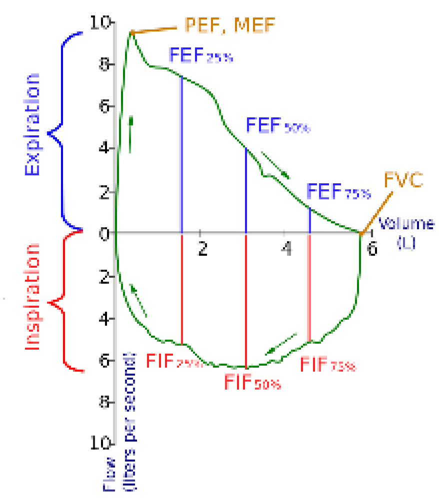


https://www.youtube.com/watch?v=o9EEszvO8PU

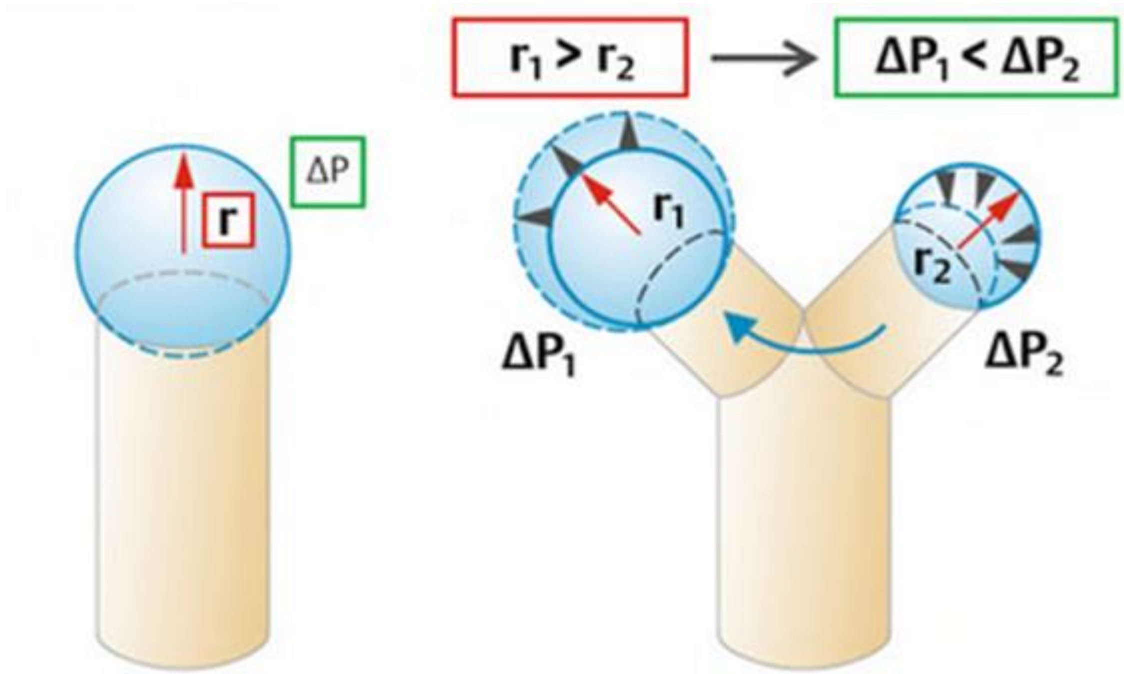
Breathing volumes







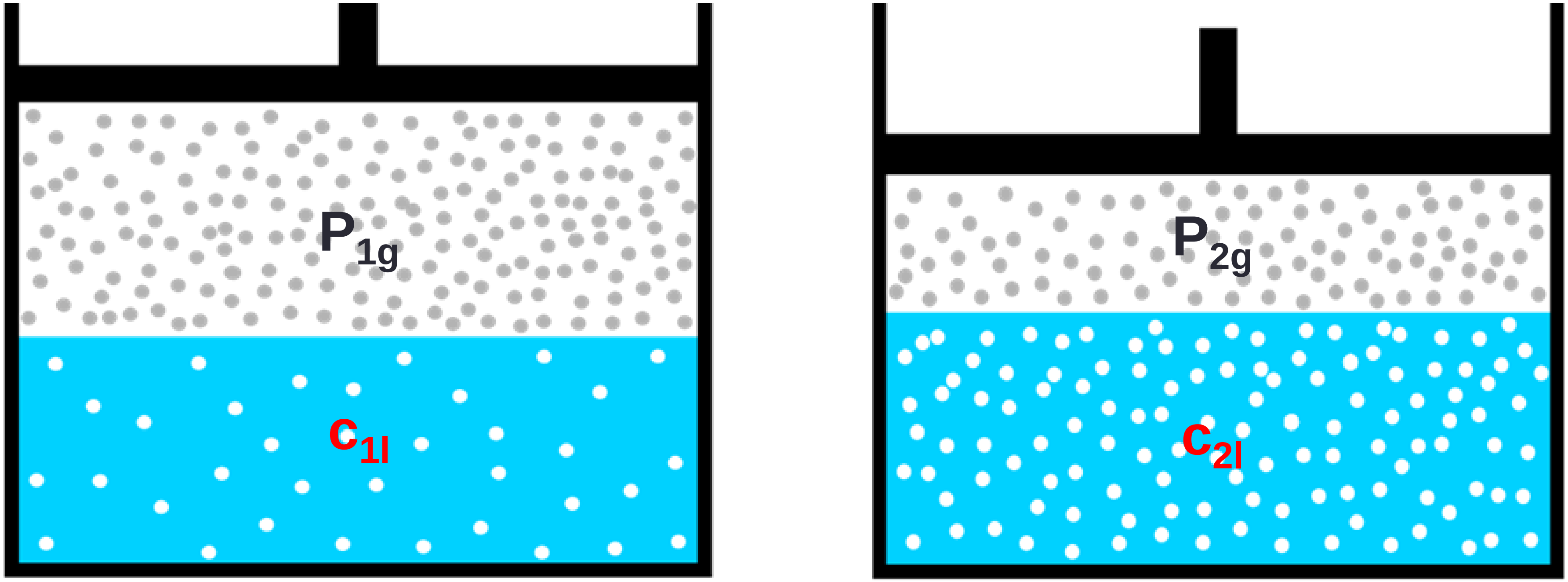
Surface tension of alveoli



$$\Delta p = 2\gamma / r$$

Surfactant reduces surface tension stronger in smaller alveoli
Damage of surfactant (e.g. during pure oxygen respiration) leads to collapse of alveoli

Gas transport – Partial pressure in liquids

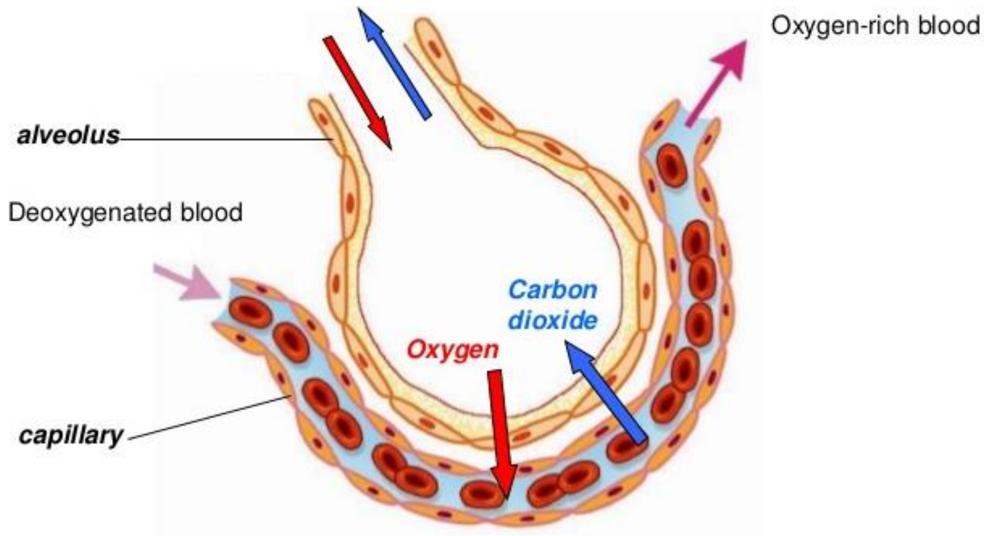


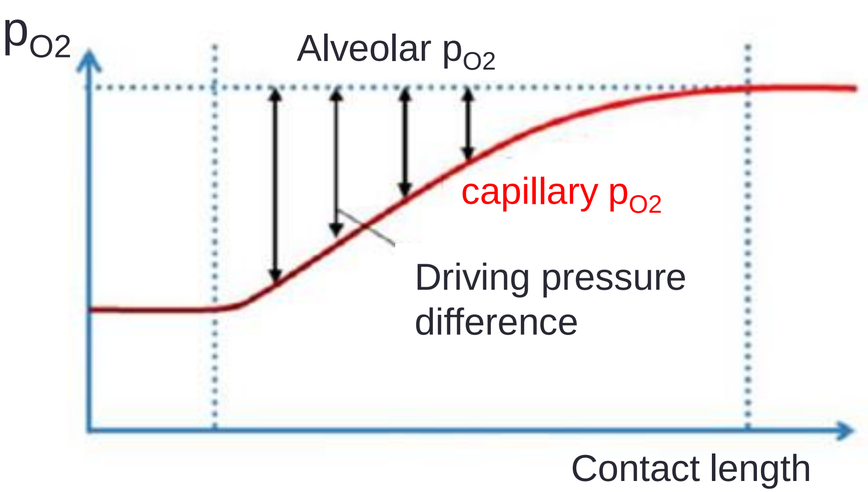
<u>Henry's law:</u>

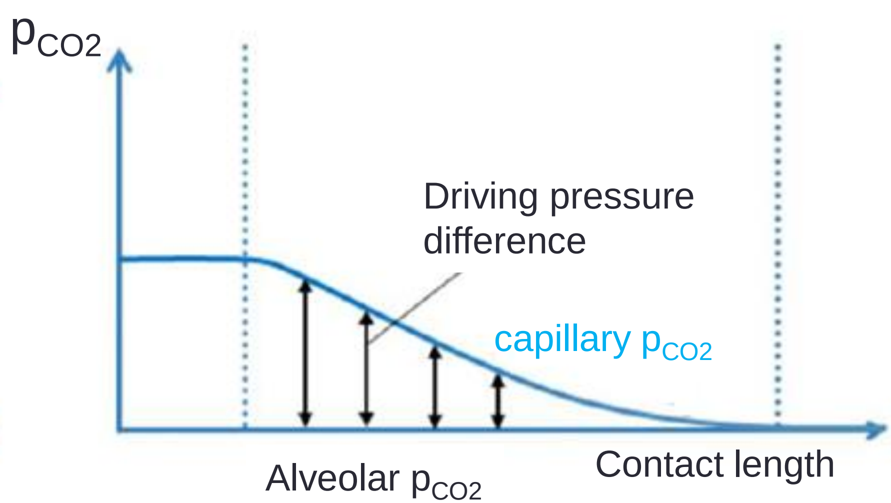
The amount of dissolved gas is proportional to the partial pressure of the gas phase

E.g. 21% of O_2 in air results in O_2 partial pressure of p_{O2}= 21%*760mmHg=160 mmHg

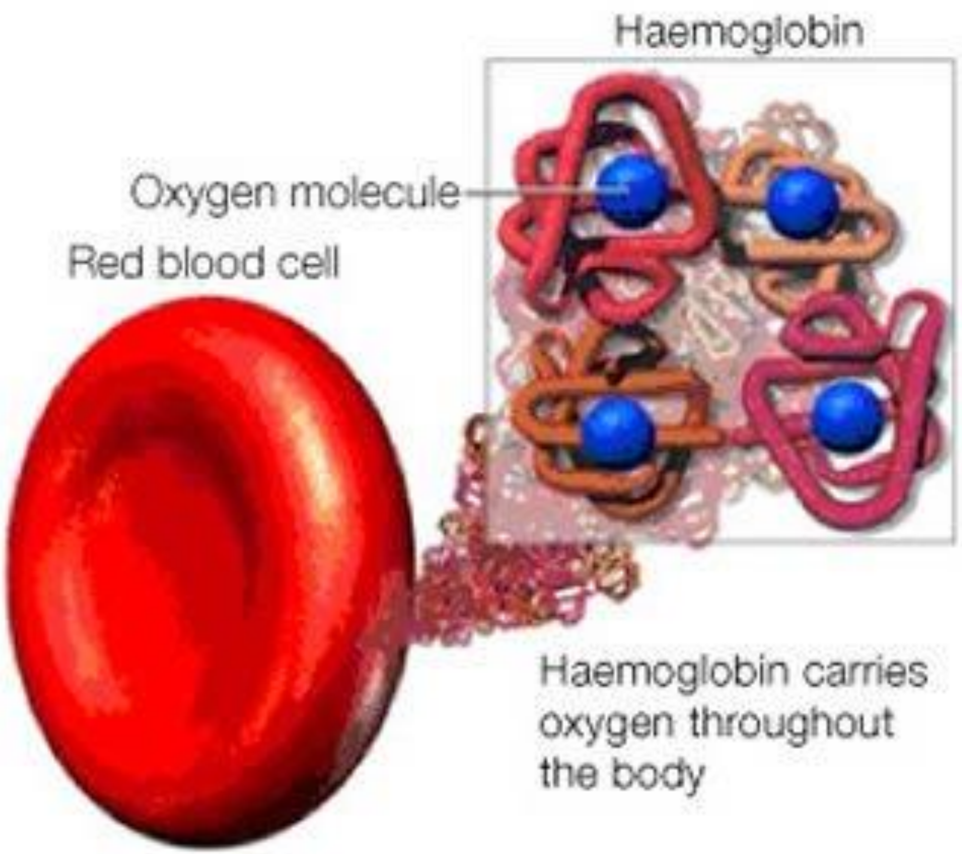
Gas exchange at alveolus







Function of Hgb

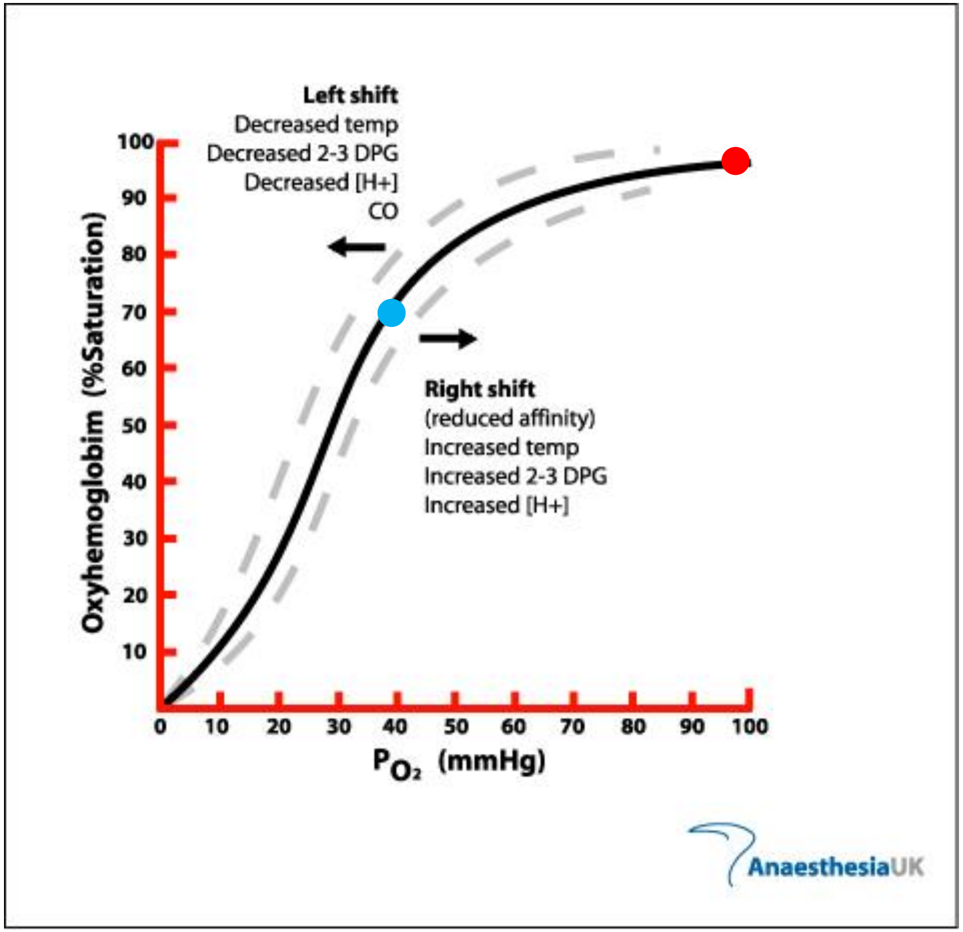


Oxygen binds to Fe sites of the Heme groups
(affinity dependent binding)

CO has 200x affinity than O_2
Risk of suffocation!

	Air	Alveolus	Ven. Blood	Art. Blood
p_{O2} [mmHg]	160	100	40	95
p_{CO2} [mmHg]	2	39	45	41

Oxygen dissociation curve

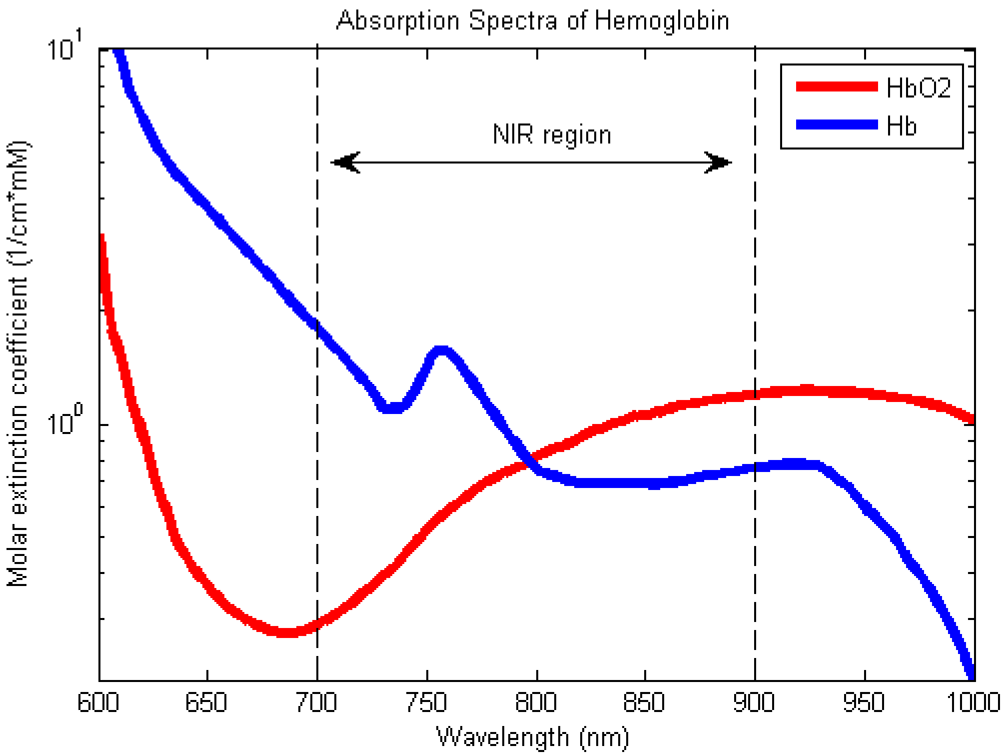


Temperature dependent!
Fever: higher oxygen demand by organs → lower oxygen affinity
Hypothermia: low metabolism → higher oxygen affinity

Surgeries in hypothermic conditions

Light hypothermia 32-37 C – Many surgeries

Mid and deep hypothermia 18-32 C – Surgeries on aorta or neo-natal surgeries



Pulse oximetry measures absorption of oxygen loaded and non-loaded Hb

Summary

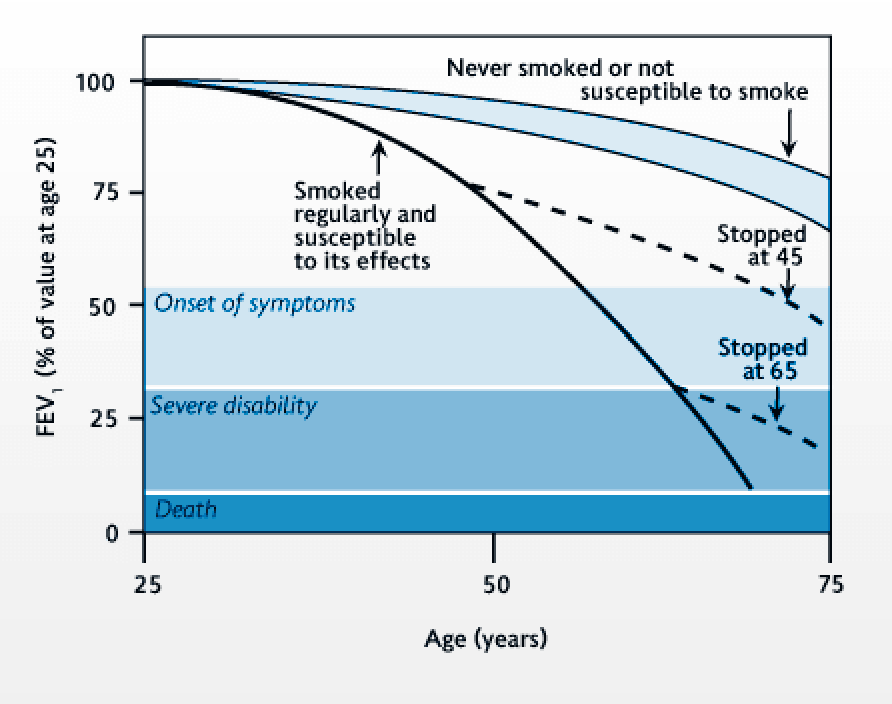
- Lung as input and output of air (pump)
- Alveoli as functional units for diffusion-based gas exchange
- Partial pressures drive the gas exchange
- Temperature (and also CO2/ pH dependence)

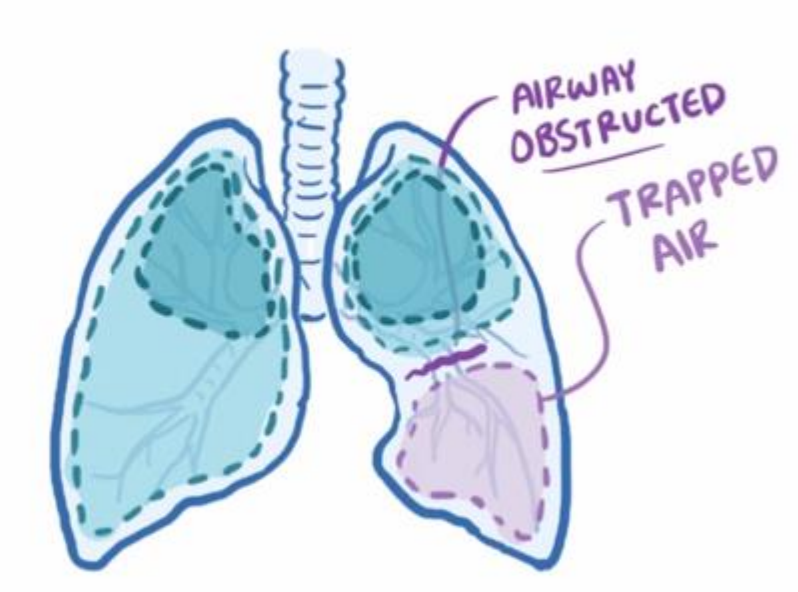
- Bicarbonate-buffer system, lactate production etc.

Questions?

Pathologies

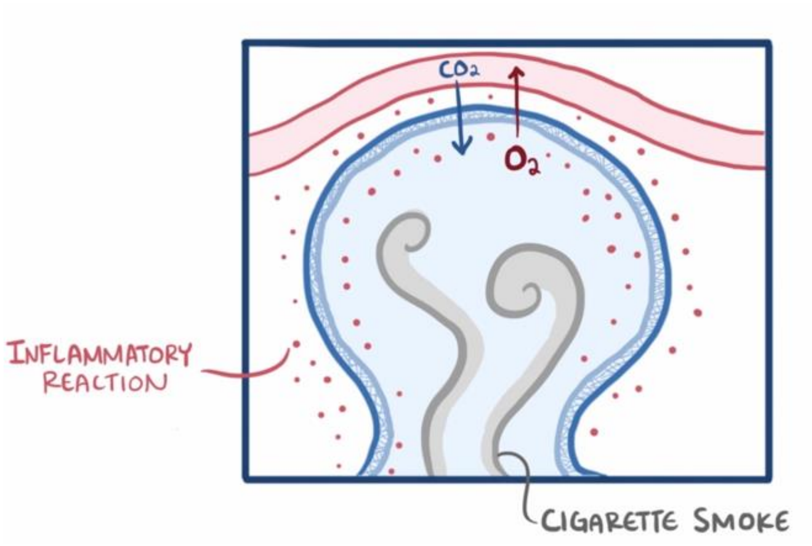
Asthma, Pneumonia,
Acute Respiratory Distress Syndrome (sudden lung trauma)
Chronic Obstructive Pulmonary Disease (**COPD**)
Respiratory failure following cardiac arrest

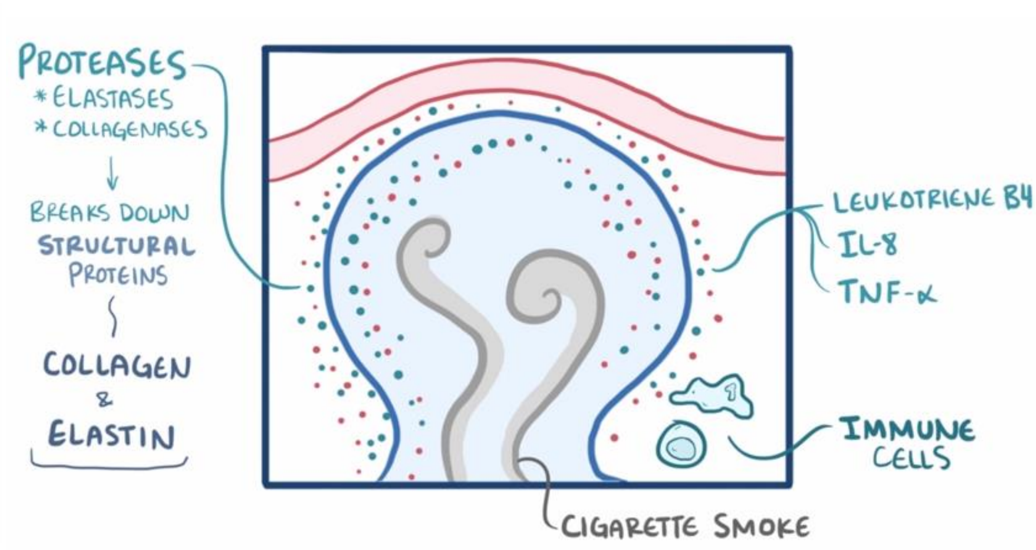


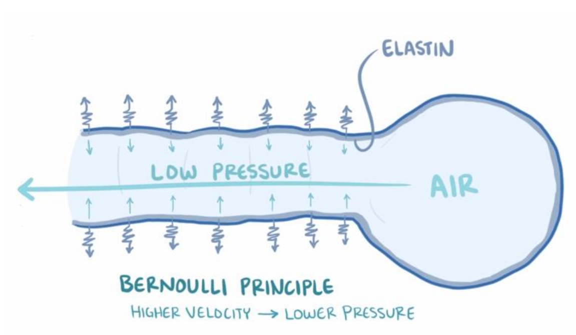


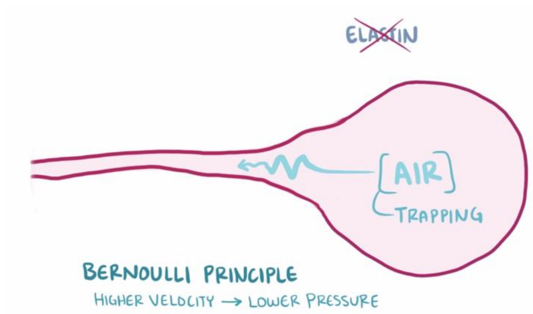
Affects 170 Mio people with costs of 2.1 trillion $

Mechanics of COPD – Emphysema development









Therapy

Change of life-style, medication, mechanical ventilation

Oxygenators (ECMO) –
Bridge to Recovery, Bridge to Transplantation, Destination Therapy

Components for ECMO

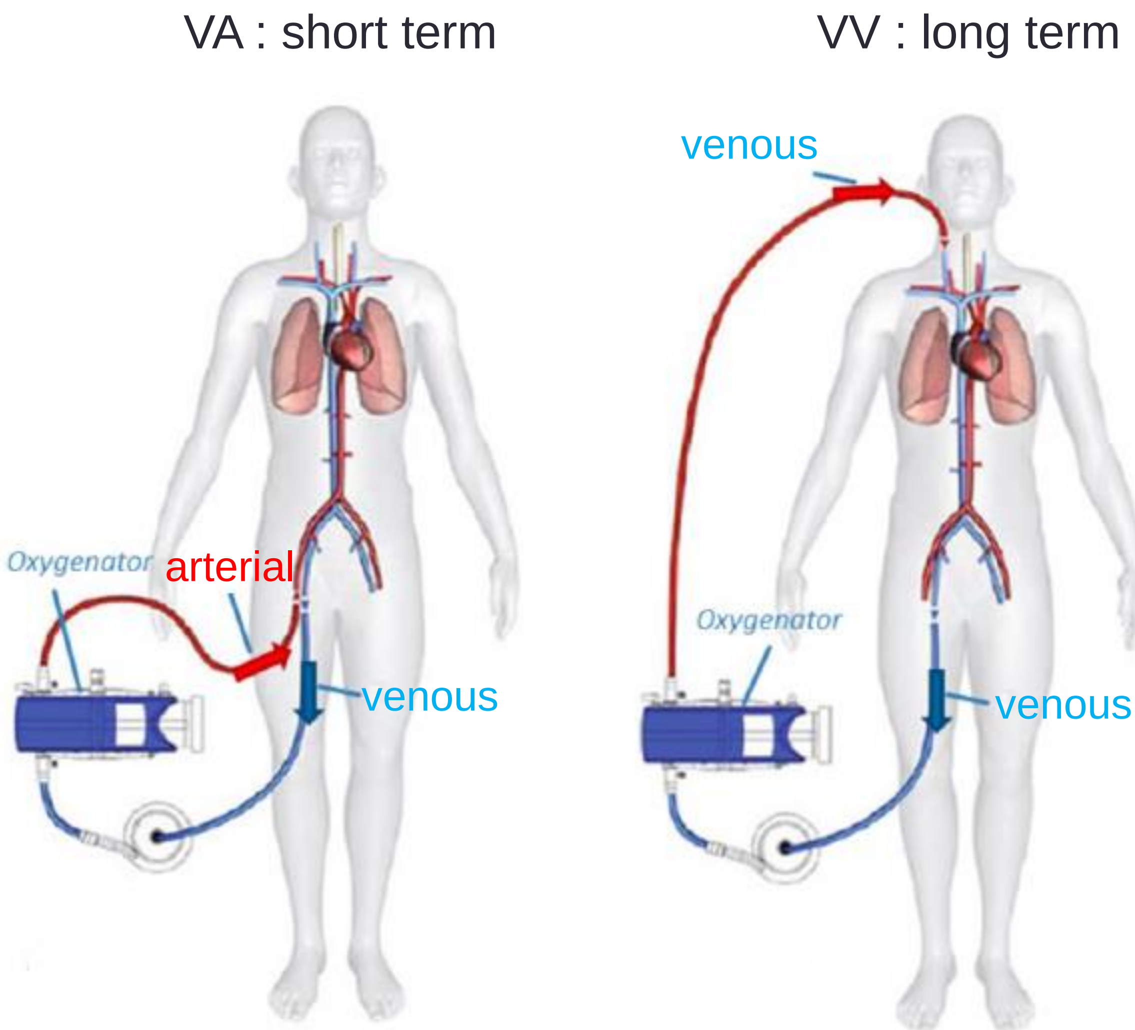
Pump

Heat Exchanger

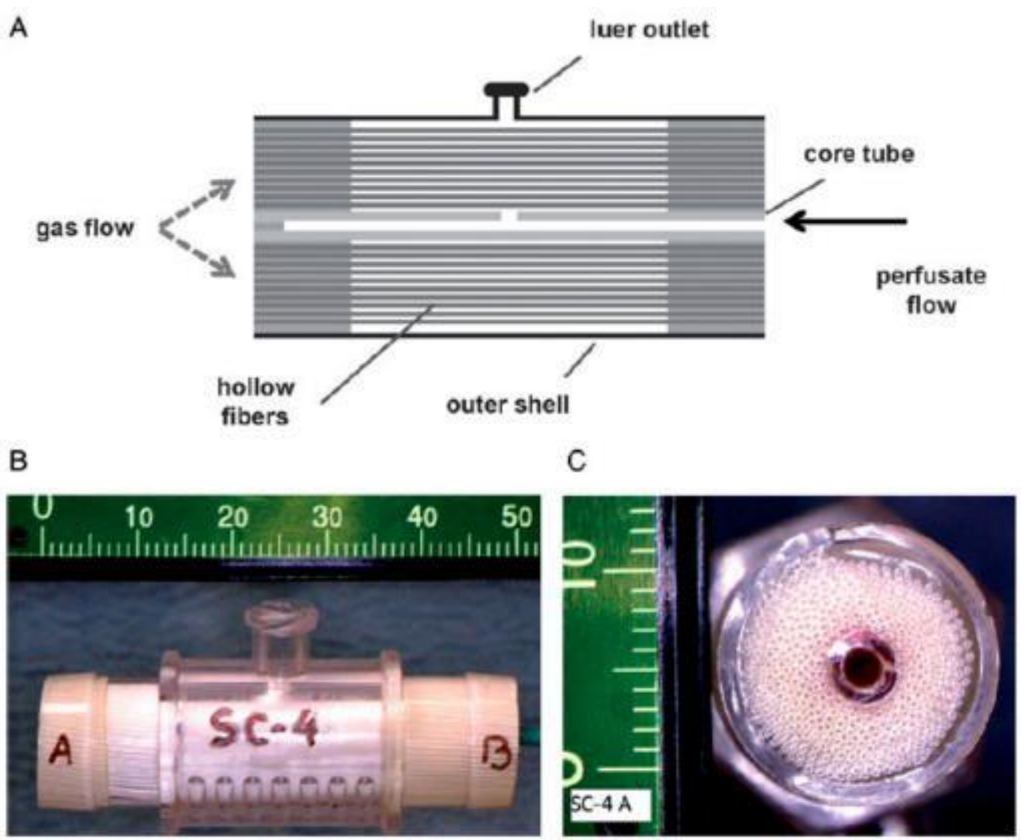
Tubing

Oxygenator

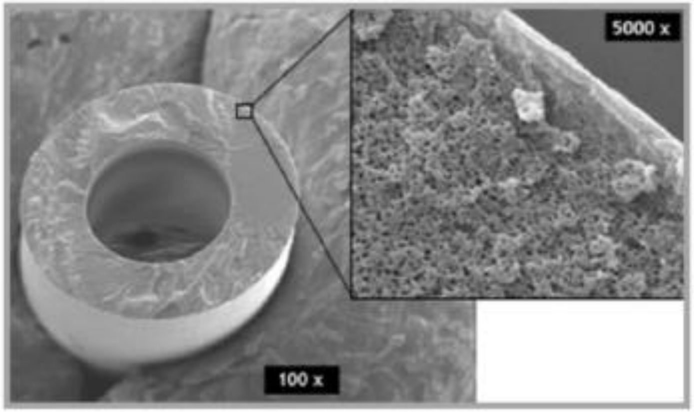
Connection possibilities



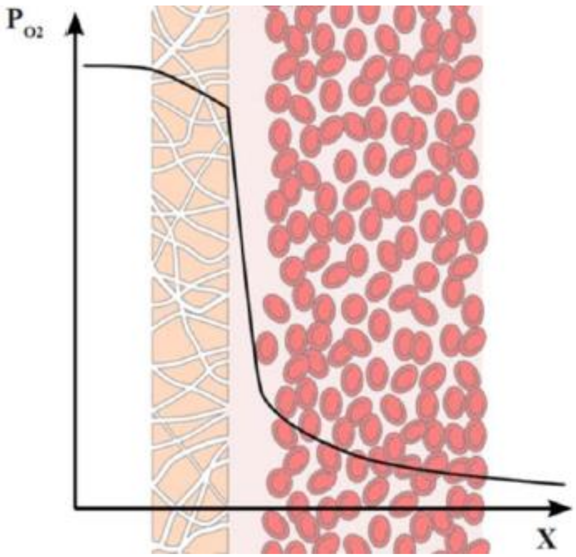
Oxygenator in detail



Gas through fibres
Blood outside of fibres



Microporosity for gas transfer



Oxygenators

Main challenge: Mobility during BTT/DT

Normally 8-10 days up to 90 days
BUT there are
patients waiting 1.5 years for organs
and in need of ECMO!

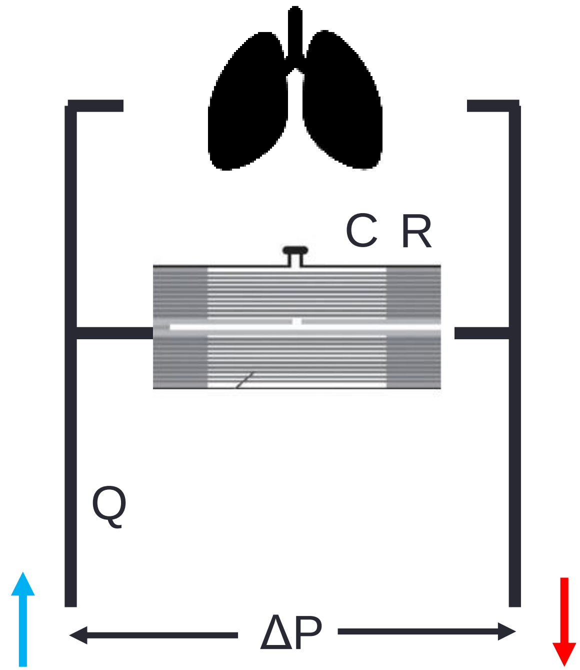
Future trends

enmodes

Paracorporeal Ambulatory Assist Lung
University of Pittsburgh

New concept of lung support from
biomechanical understanding of the lungs

Mechanics of (long-term) lung support

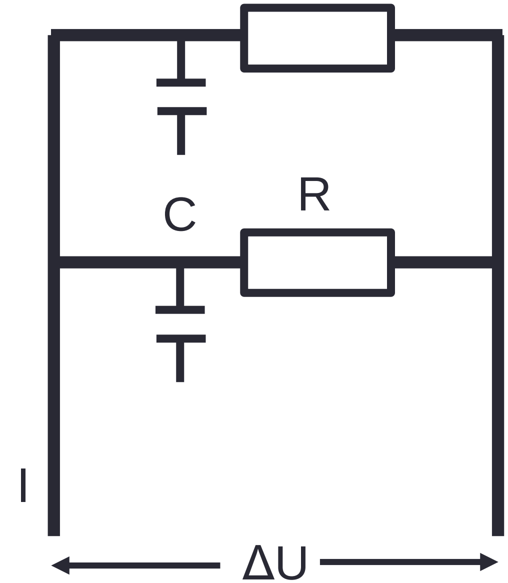


Pulmonary
Artery

Left
Atrium

$$\frac{dp}{dt} = \frac{Q}{C}$$

$$R = \frac{\Delta p}{Q}$$

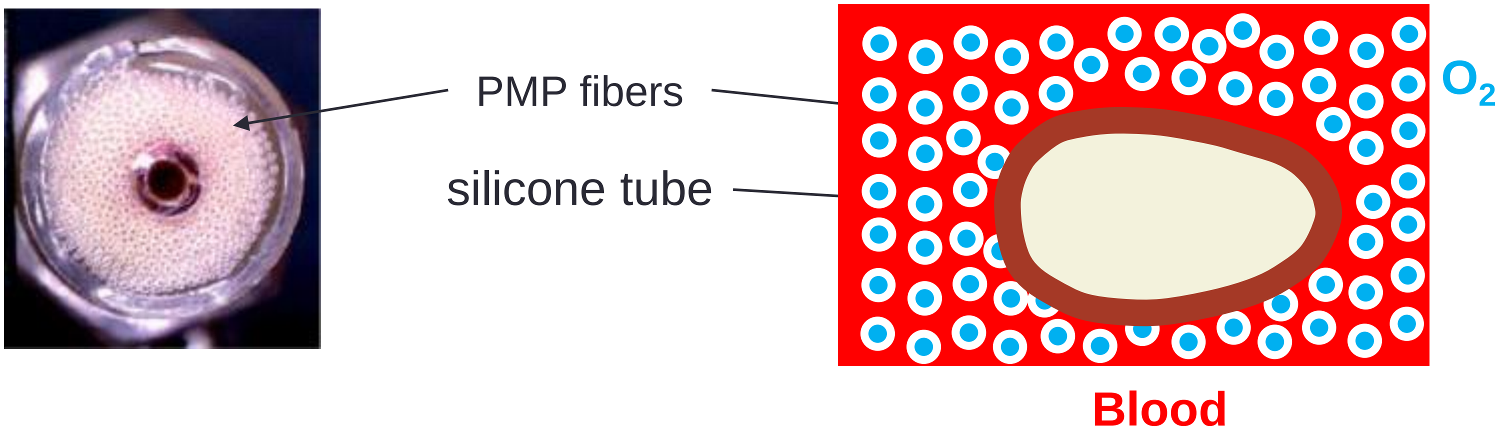


Capacitor ←→
Vascular compliance

Resistor ←→
Vascular resistance

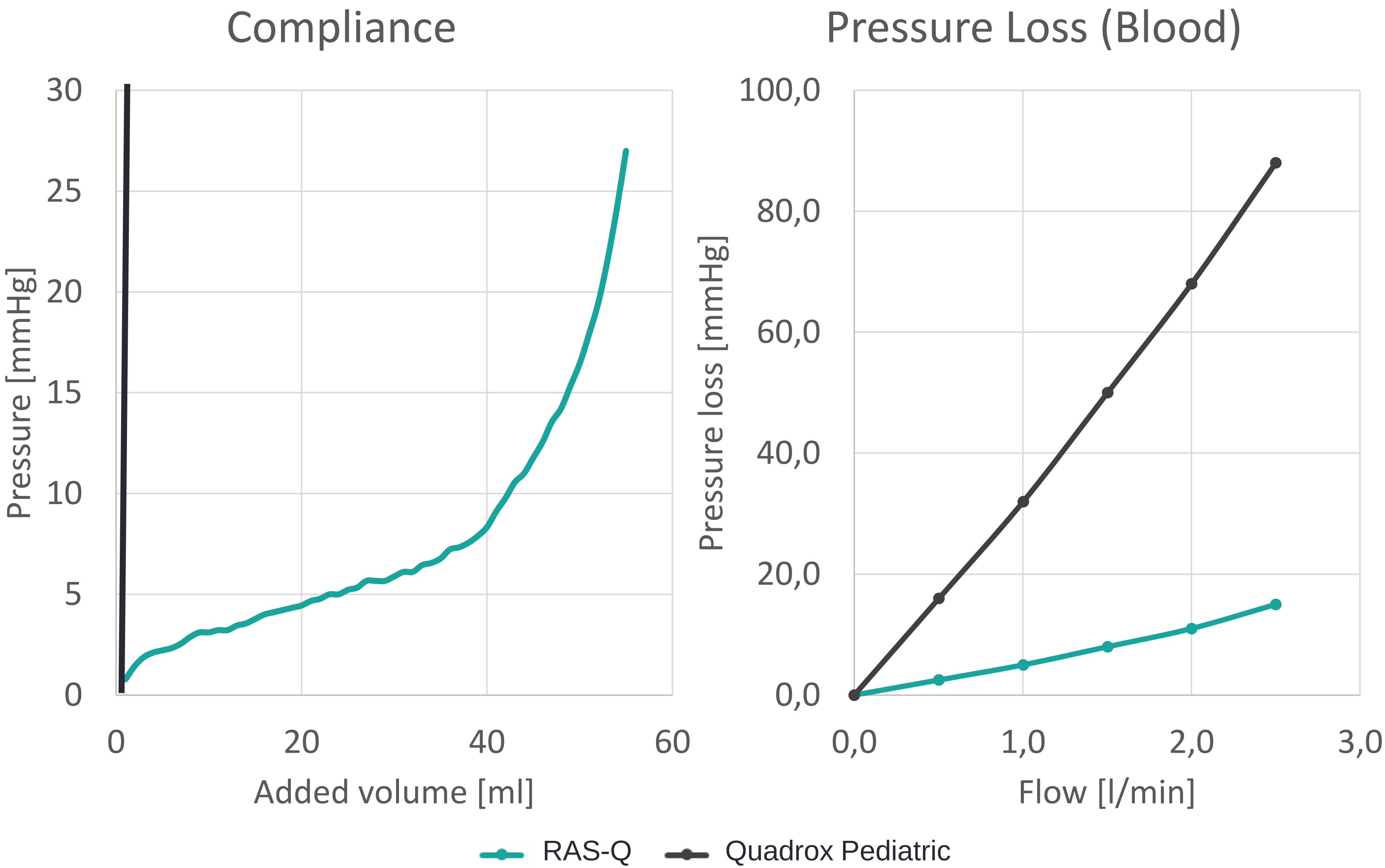
C ↑ ➔ pressure peaks are damped ➔ resistance is lower ➔ Q_{mean} is higher

Principle design and in vitro test



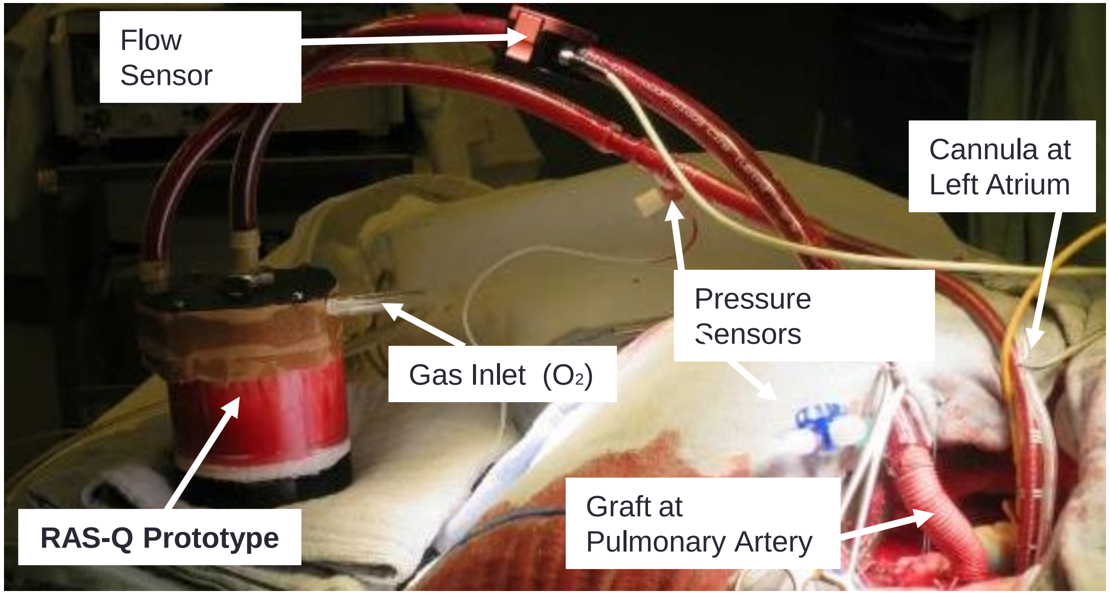
Measure the compliance (ΔV/Δp) and blood flow/pressure drop in a hydraulic circuit

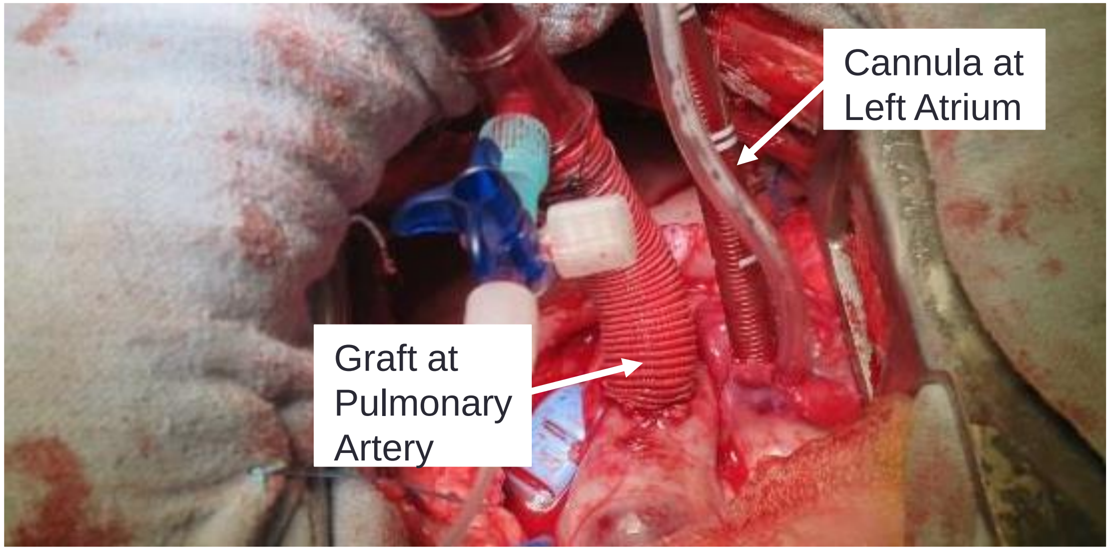
Results – *in vitro* (n=9)



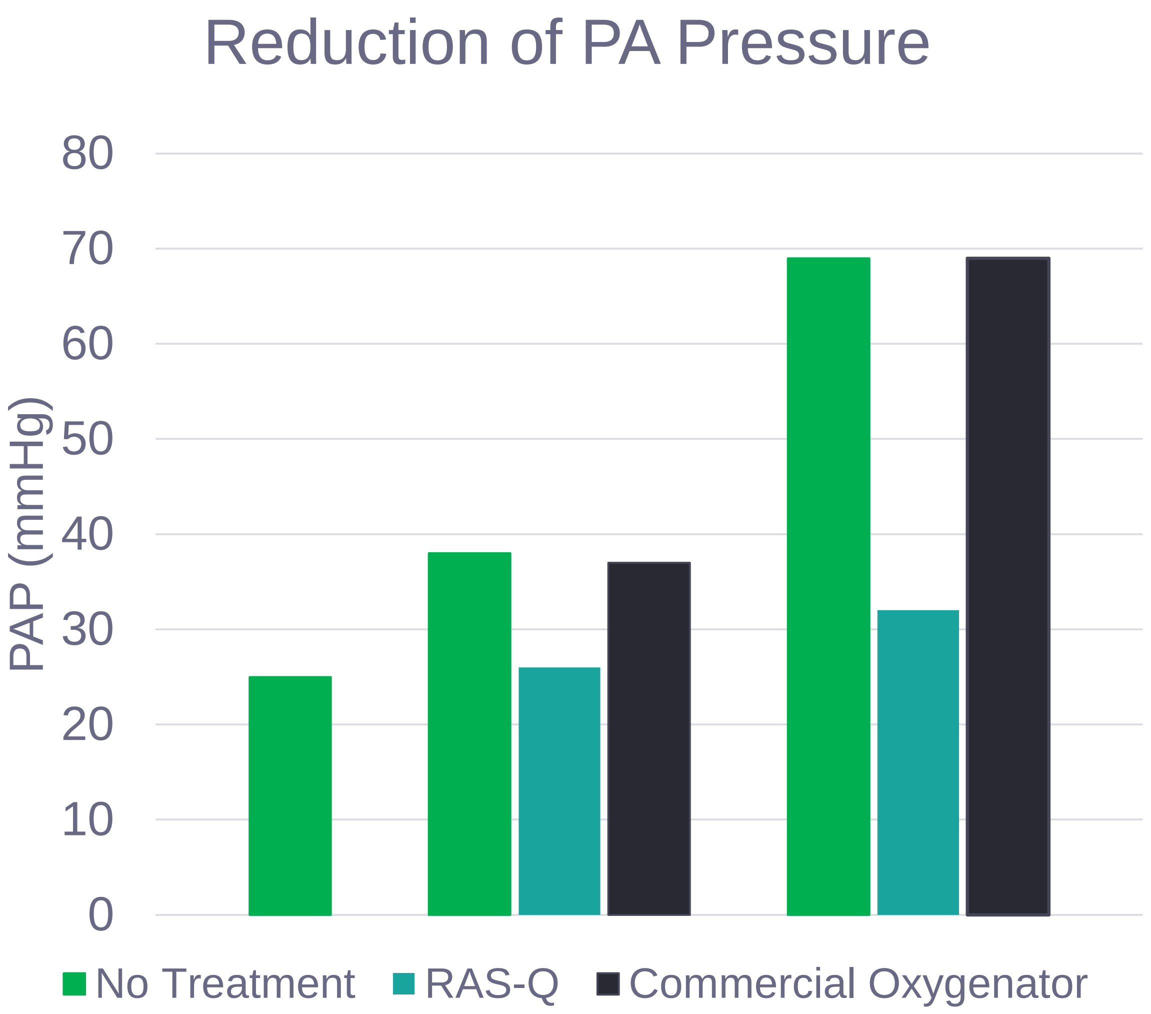
Acute animal trials

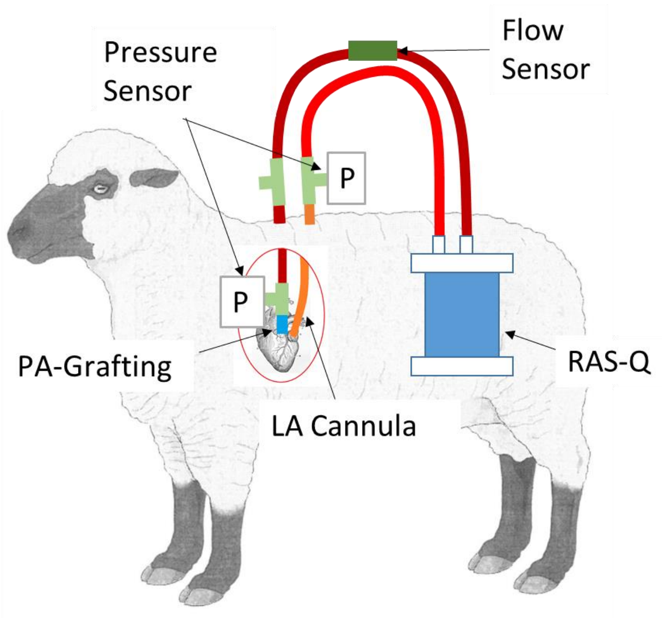
- Four acute animal tests (sheep, 53±7kg)
- No pump
- Banded the PA
- Measured PA pressure and flow with and without RAS-Q



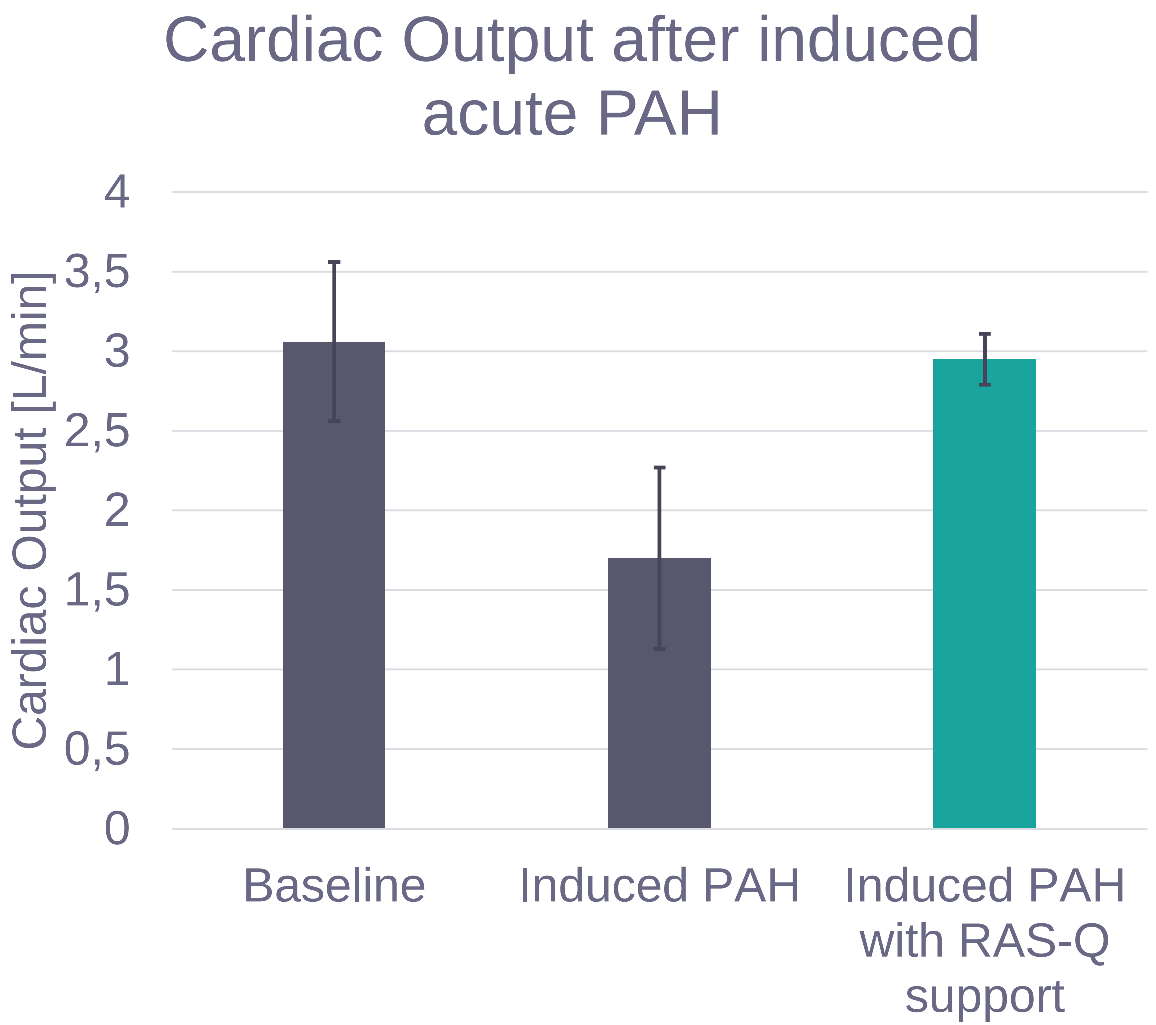


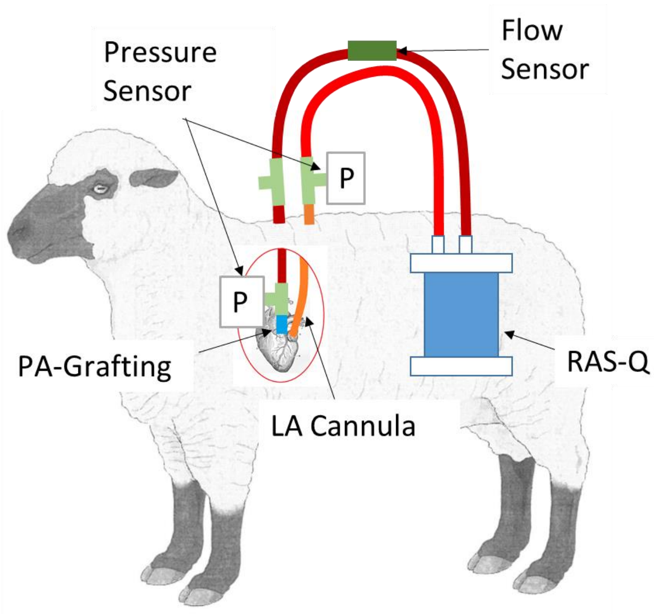
Results – in vivo (n=4)





Results – in vivo (n=4)





Take home message

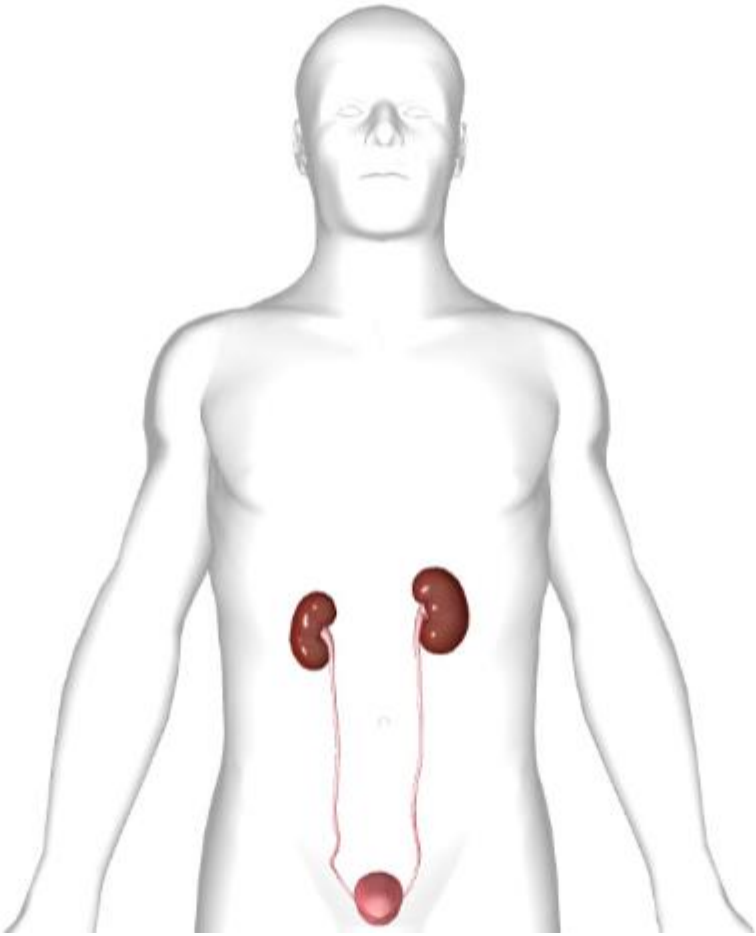
- Important to **understand** the basic biomechanical behavior of the body for development of **new devices/therapies**
- Think about the patient ➔ in the beginning ECMO allowing mobility ➔ Now ideas of apply the device for PAH or COPD!
- The biomedical field has still **many possibilities** for innovations which can be achieved even with small teams. Ras-Q development by 1 post-doc (and undergrads)

2014	2015	2016	2017+
Idea, In vitro tests Proof of principle Proof of concept	Design optimization Design freeze of prototype	Acute animal trials (short term) Funding & Partners	Chronic animal trials Applications First-in-man Market entry

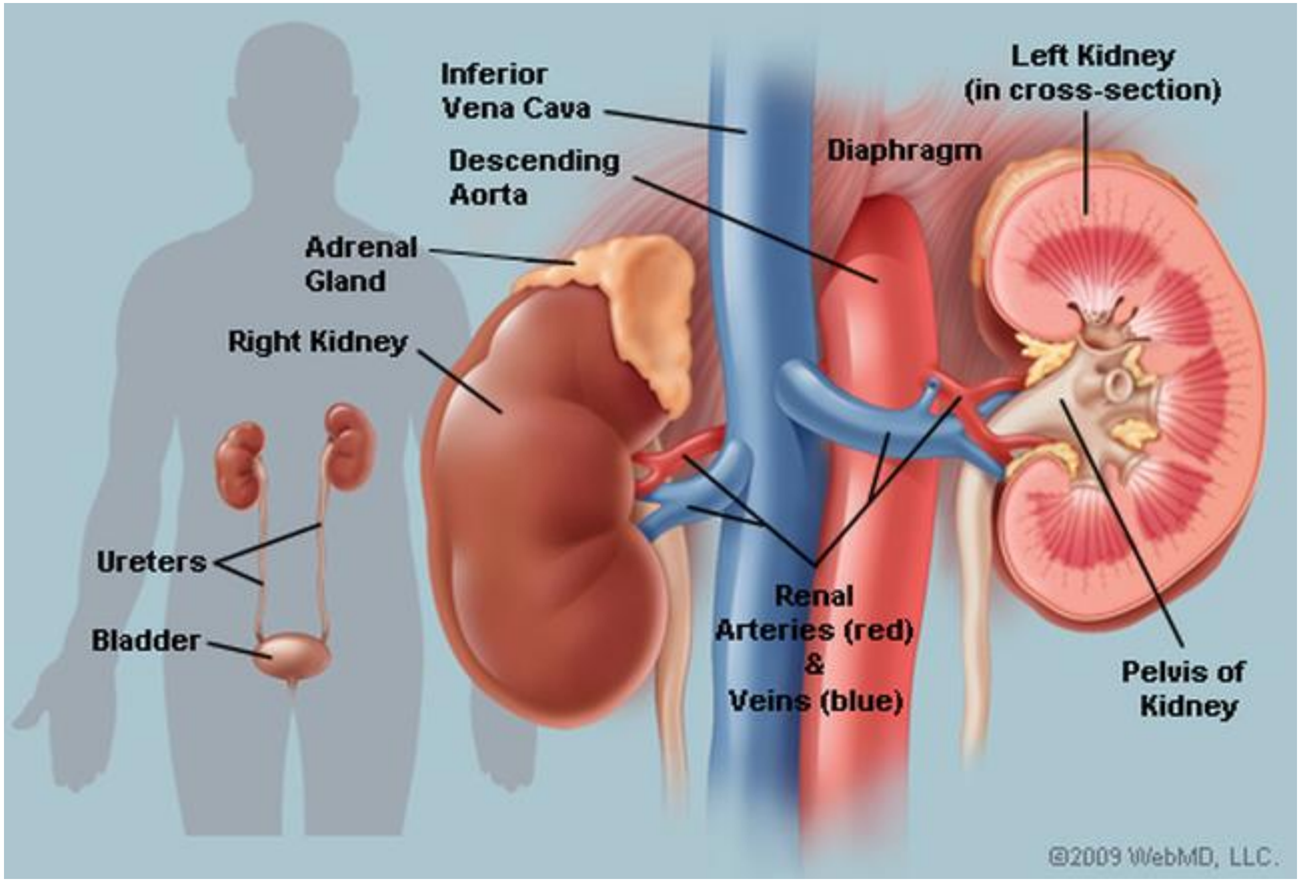
RAS-Q
ONE BREATH AHEAD

Questions?

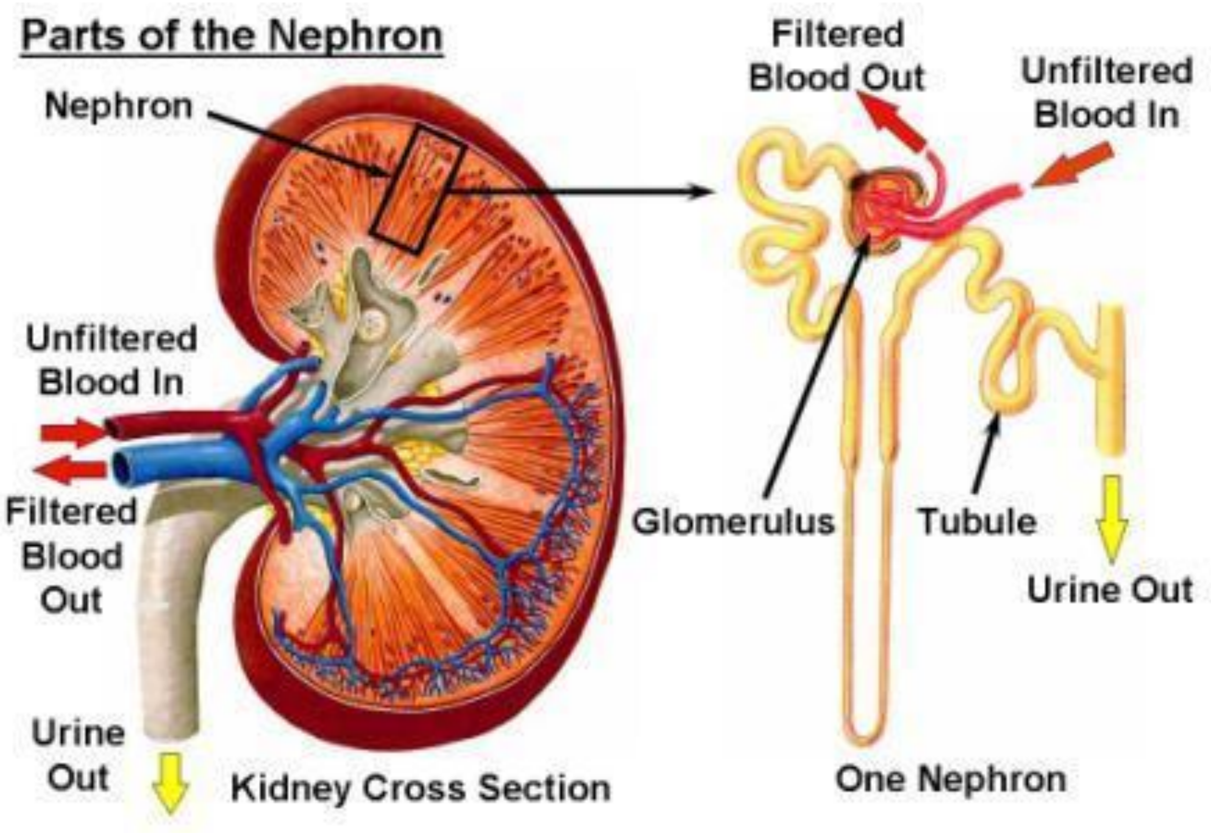
Renal System



Anatomy and Physiology



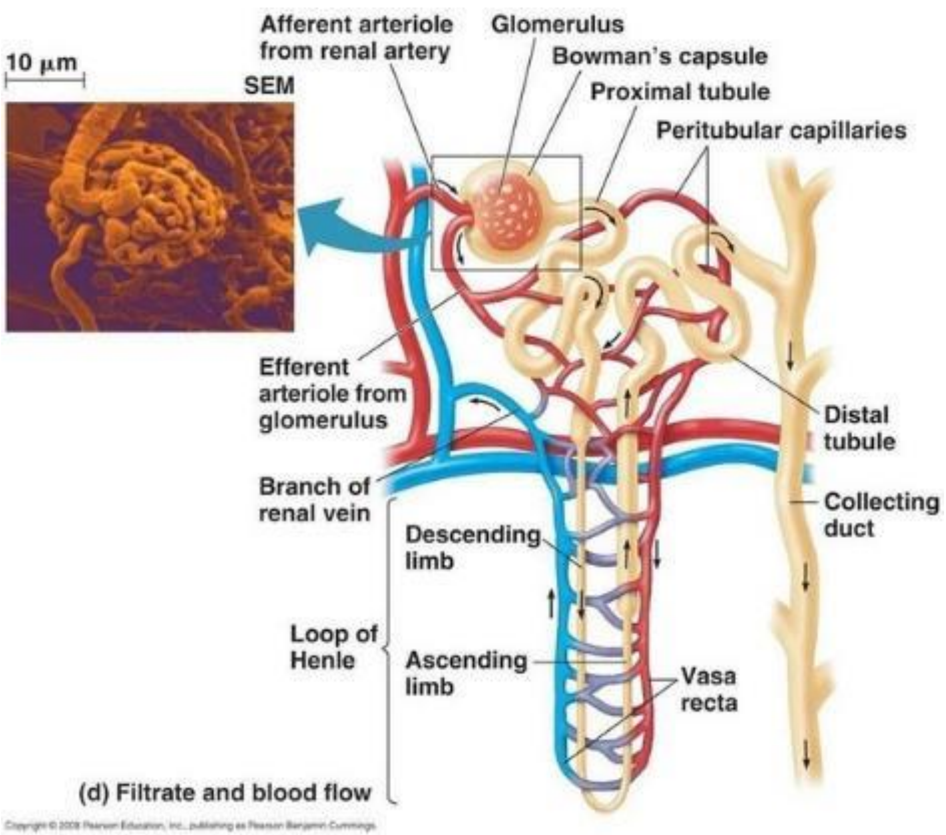
Blood Supply and Functional Unit

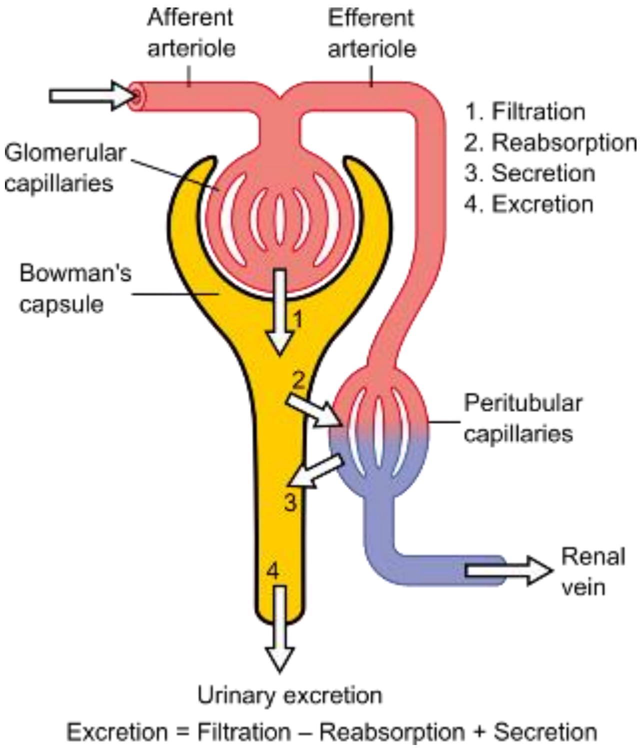


Nephron is the functional unit that removes waste and controls body fluid and electrolyte in blood, regulates blood pressure

About 1 Mio in each kidney

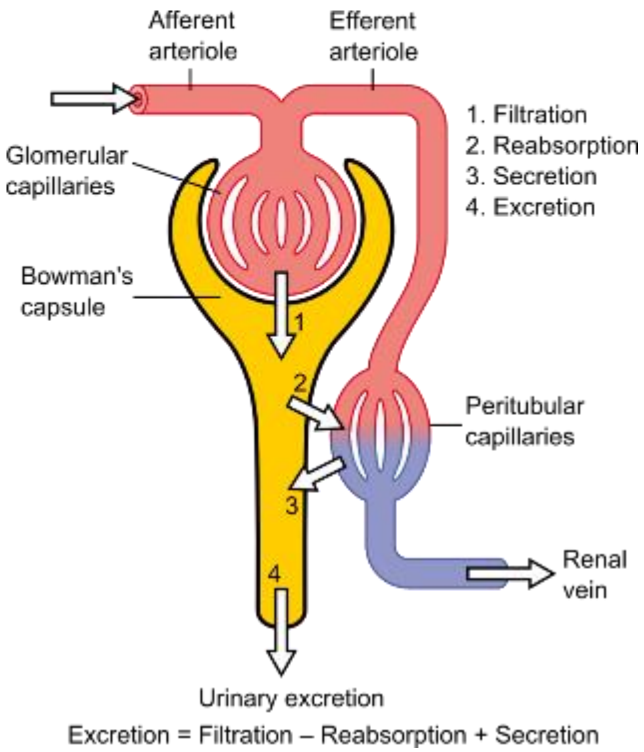
Physiology of the nephron





Simplification of the urinary excretion tract

Working principle



1. Step - **Ultrafiltration** by pressure gradient removal of water, glucose, proteins, urea

2. Step – **Reabsorption** by pressure gradient Diffusion and active transport of glucose, proteins, water back to the blood

3. Step – **Secretion** (active and passive) of molecules from the blood

4. Step – Final excretion

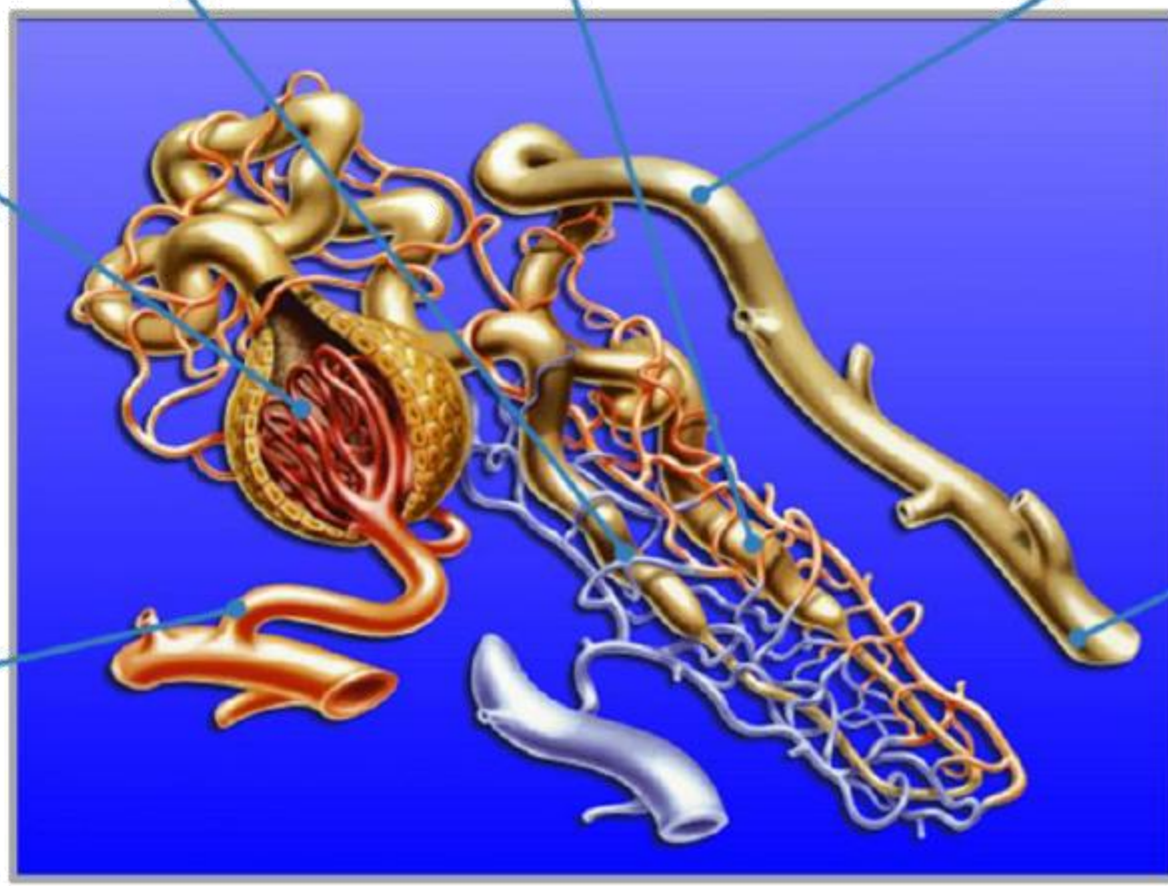
Fluid volumes

60 l of urine per day at end of prox. tubuli

20 l of urine per day at of dist. tubuli

20 l of urine per day at end of dist. tubuli

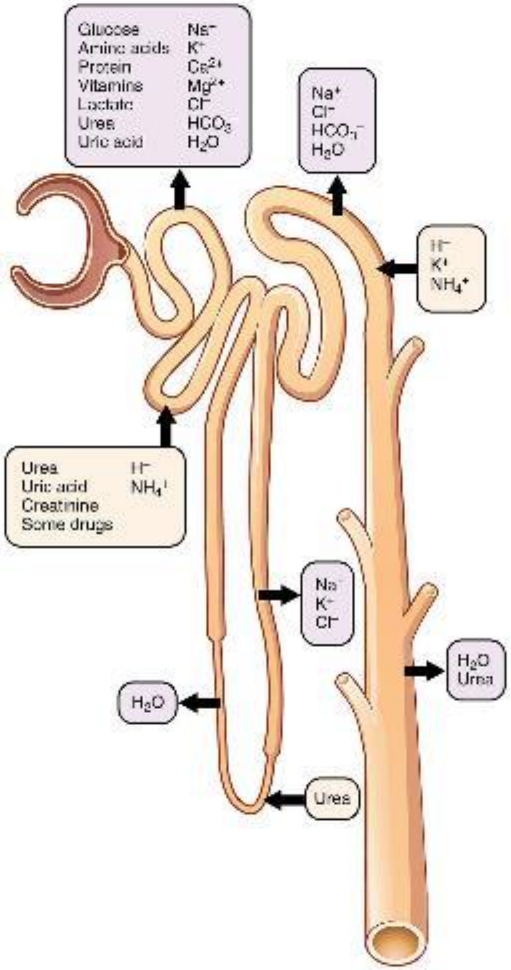
180 l of filtrate per day in glomeruli



1.5 l of urinary excretion

1800 l of blood per day

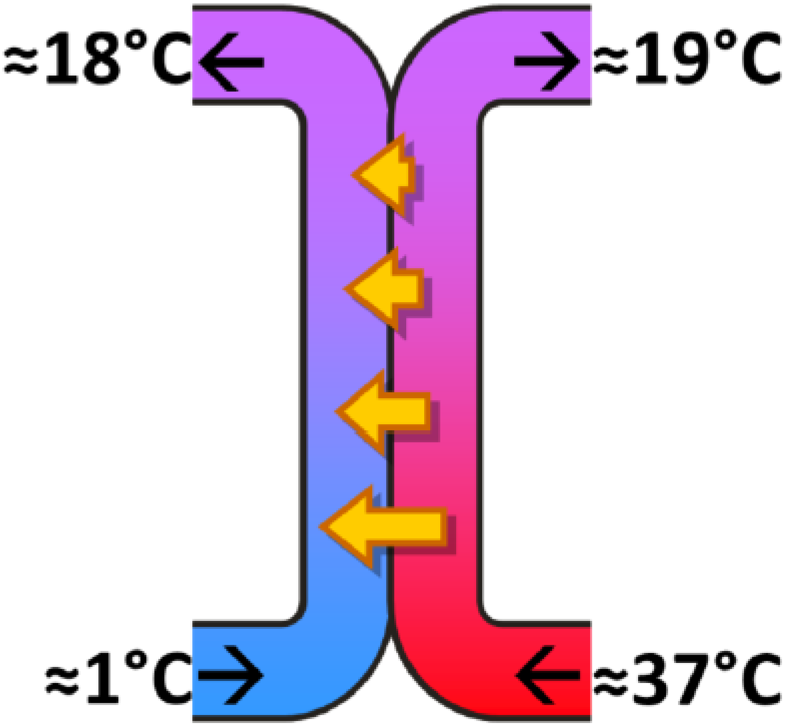
Complex regulatory apparatus



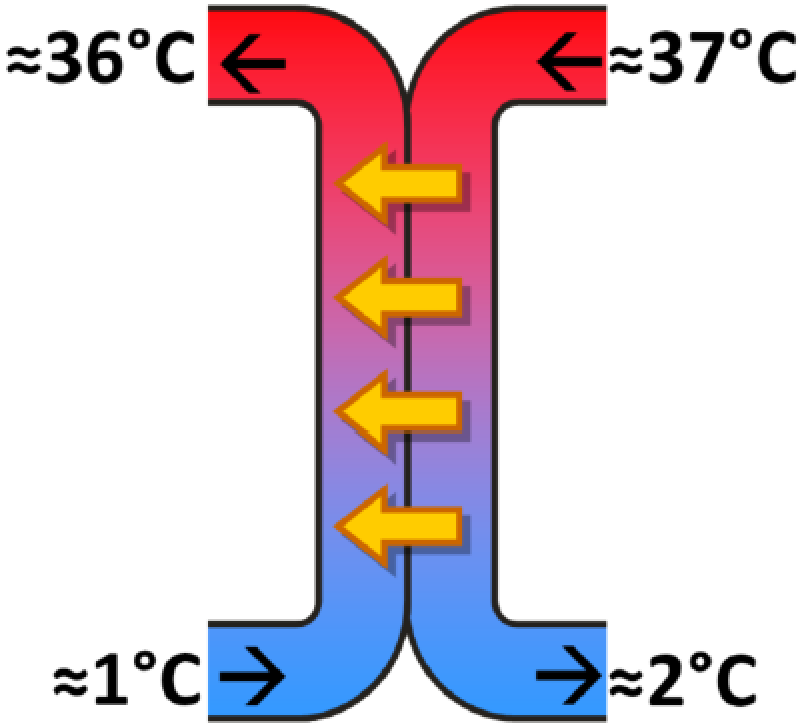
What is the exchange principle in the kidney?

Heat or Mass transfer

Cocurrent flow



Countercurrent flow



Constant gradient to overcome

Summary

Kidney to clean blood and regulate its components

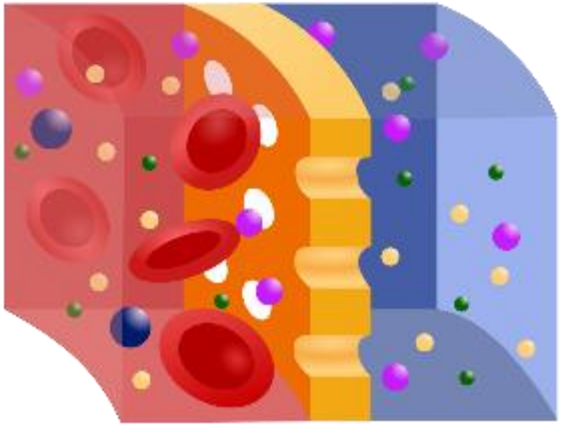
Combination of diffusion, osmosis and filtration

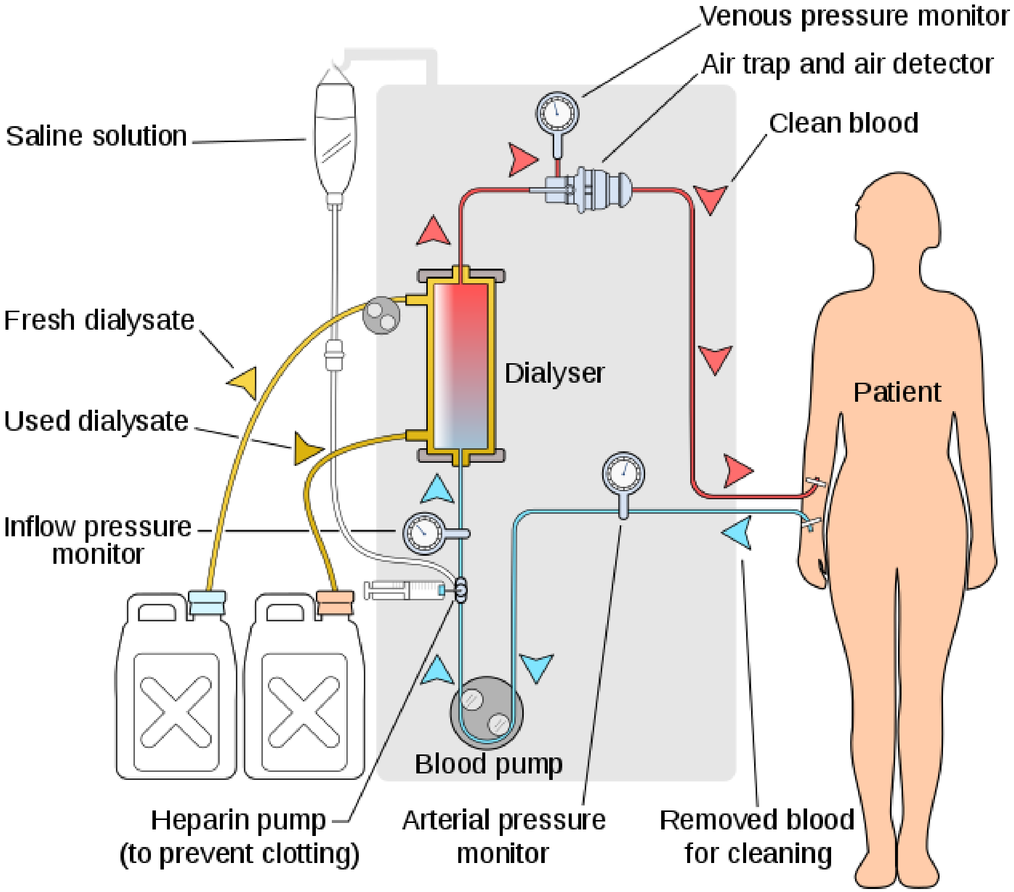
High throughput (1700 l/day) → Failure is dramatic

Pathologies

- Inflammatory (Glomeruli, interstitial tissue, tubules)
- Congenital diseases
- Trauma, tumor etc.

Hemodialysis





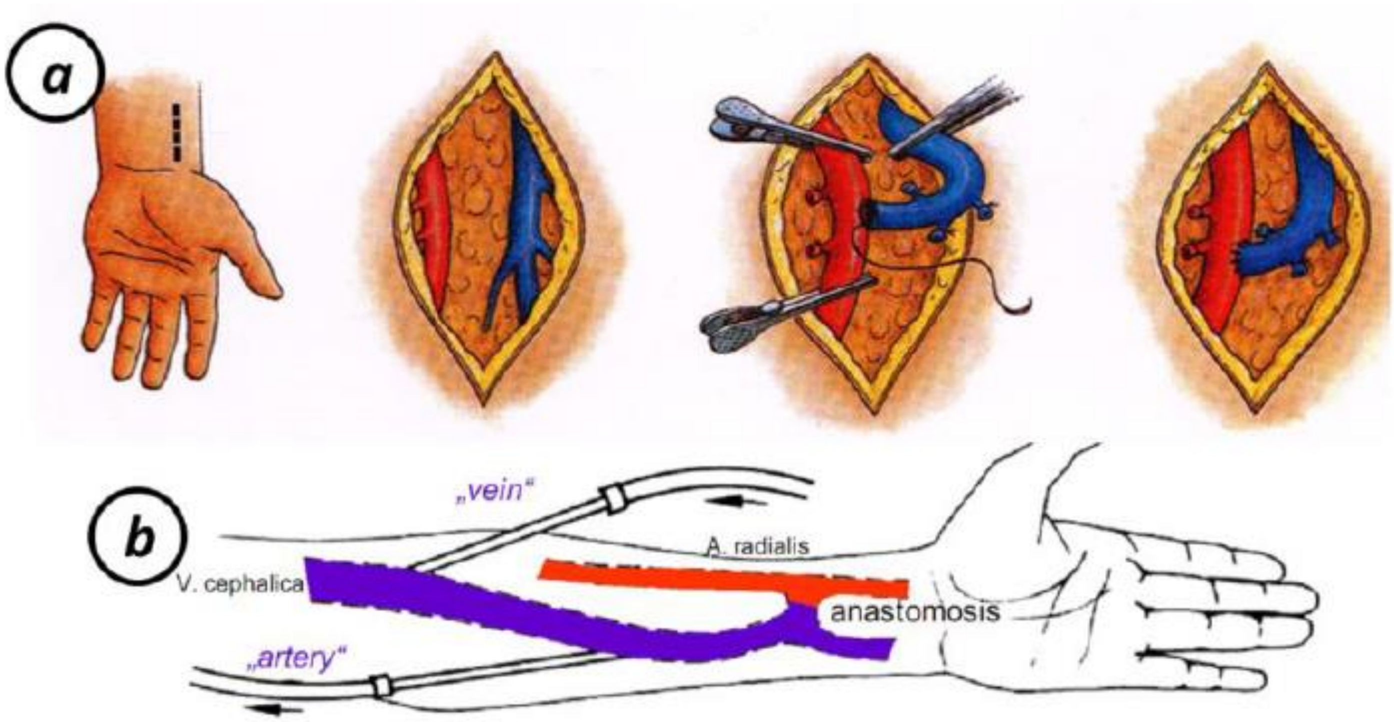
Dialysis Filter

https://www.youtube.com/watch?v=71XNJekYV5o

What about connection?

3/week 4-5 hours 200ml/min → easy and painless connection principle necessary

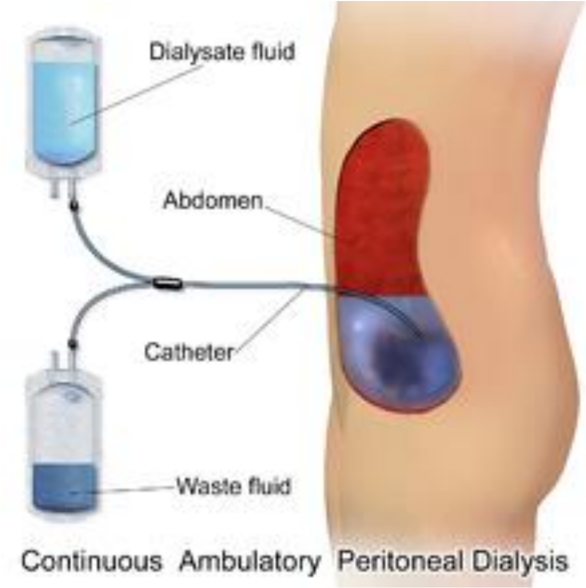
Use veins instead of arteries, BUT veins in e.g. arm do not carry enough blood



Anastomosis (Cimino Shunt) for long term use

Other kinds of dialysis

Hemofiltration for ICU
Convection instead of diffusion



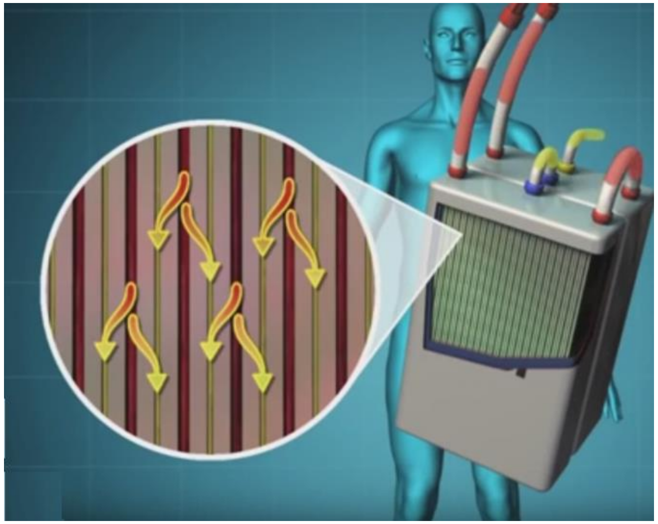
Peritoneal dyalisis (10% of the cases)

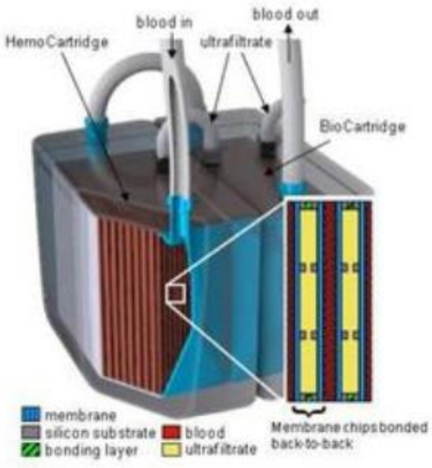
Research: Artificial Kidney

Affects about 2 Mio people worldwide

About 40 bio $ for US patients with ESRD and traditional dialysis

Need to find a better way for Bridge to Transplantation or Destination Therapy





UCSF, University of California, San Francisco

Summary of Lecture

- Heart : Pump, Lung: Air Supply, Kidney : Waste
- Interconnected System : Failure/malfunctioning of one component will affect the others
- Transplantation is the gold standard for end stage diseases
- Basic mechanical principles are enough to understand the system and develop devices
- Patient mobility, BTT and DT(!) are the next steps

Sources

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